	L #	Hits	Search Text	DBs	Time Stamp
1	L1	53688	antibody or mab or moab or monoclonal	USPAT	2003/02/14 10:55
2	L2	86252	glycerophospholipid or (fatty adj acid) or saccharide or glycerol-3-phosphate or dimysteroylphosphatidic or dimysteroylphosphatidylcholine or distearoylphosphatidic or distearoylphosphatidylcholine or glucoside	USPAT	2003/02/14 10:58
3	L3	8334	1 and 2	USPAT	2003/02/14 10:58
4	L4	4088	435/7.1.ccls.	USPAT	2003/02/14 10:58
5	L5	439	3 and 4	USPAT	2003/02/14 10:58
6	L6	5573	fluorescen$3 adj intensity	USPAT	2003/02/14 11:15
7	L7	43	5 and 6	USPAT	2003/02/14 10:59
8	L8	362	4 and 6	USPAT	2003/02/14 11:11
9	L9	44	8 and 2	USPAT	2003/02/14 11:11
10	L11	5447	dimysteroylphosphatidic or dimysteroylphosphatidylcholine or distearoylphosphatidic or distearoylphosphatidylcholine or glucoside or thioglucoside	USPAT	2003/02/14 11:13
11	L12	3	9 and 11	USPAT	2003/02/14 11:13
12	L13	320	fluorescen$3 adj intensity same enhanc$5	USPAT	2003/02/14 11:15
13	L14	4088	435/7.1.ccls.	USPAT	2003/02/14 11:16
14	L15	19	13 and 14	USPAT	2003/02/14 11:16

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(FILE 'HOME' ENTERED AT 11:28:44 ON 14 FEB 2003)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 11:29:05 ON 14 FEB 2003
L1 11902 S INDOCYANINE GREEN
L2 3689 S FLUORESC? ENHANCE?
L3 6 S L1 AND L2
L4 3 DUP REM L3 (3 DUPLICATES REMOVED)
L5 43654 S GLUCOSIDE OR THIOGLUCOSIDE
L6 12 S L2 AND L5
L7 6 DUP REM L6 (6 DUPLICATES REMOVED)

FILE 'REGISTRY' ENTERED AT 11:37:28 ON 14 FEB 2003
L8 0 S INDOCYANINE GREEEN
L9 3 S INDOCYANINE GREEN

FILE 'REGISTRY' ENTERED AT 11:40:02 ON 14 FEB 2003
L10 1 S 28782-33-4/RN
SET NOTICE 1 DISPLAY
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FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 11:42:38 ON 14 FEB 2003
L11 13141 S 4,5-BENZOINDOTRICARBOCYANINE OR CARDIO GREEN OR INDOCYANINE G
L12 6 S L11 AND L2
L13 3 DUP REM L12 (3 DUPLICATES REMOVED)
L14 29182 S SACCHARIDE
L15 2 S L14 AND L2
L16 2 DUP REM L15 (0 DUPLICATES REMOVED)
L17 366372 S FATTY ACID
L18 78 S L17 AND L2
L19 32 DUP REM L18 (46 DUPLICATES REMOVED)
L20 7 S L11 AND L5
L21 4 DUP REM L20 (3 DUPLICATES REMOVED)
L22 40123 S INTENSITY (3A) FLUORESC?
L23 86 S L11 AND L22
L24 42 DUP REM L23 (44 DUPLICATES REMOVED)

fluorescein concentration curve and the reference ***ICG*** curve is a measure of the accumulation of fluorescein in the disc tissue. The measurements indicate that fluorescein dye does not diffuse across the capillaries in the optic disc. The accumulation of fluorescein in the disc only starts at about 1 min after the injection and seems to be due to diffusion of the dye from the surrounding choroid. The time constant of this diffusion process was found to be approximately 1 min.

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FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 11:29:05 ON 14 FEB 2003
L1 11902 S INDOCYANINE GREEN
L2 3689 S FLUORESC? ENHANCE?
L3 6 S L1 AND L2
L4 3 DUP REM L3 (3 DUPLICATES REMOVED)
L5 43654 S GLUCOSIDE OR THIOGLUCOSIDE
L6 12 S L2 AND L5
L7 6 DUP REM L6 (6 DUPLICATES REMOVED)

FILE 'REGISTRY' ENTERED AT 11:37:28 ON 14 FEB 2003
L8 0 S INDOCYANINE GREEEN
L9 3 S INDOCYANINE GREEN

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L10 1 S 28782-33-4/RN
SET NOTICE 1 DISPLAY
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L11 13141 S 4,5-BENZOINDOTRICARBOCYANINE OR CARDIO GREEN OR INDOCYANINE G
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L22 40123 S INTENSITY (3A) FLUORESC?
L23 86 S L11 AND L22
L24 42 DUP REM L23 (44 DUPLICATES REMOVED)

to the variability of absorption of the targets were observed. Variability was related to the amount of ***ICG*** . For each curve, 3 zones were identified: (i) for fluences ranging from 60 +/- 20 J/cm2 to 110 +/- 20 J/cm2 a transient intravascular fluorescence was observed only for the loser pulses targeted on the vessels, (ii) for fluences ranging from 110 +/- 20 J/cm2 to 190 +/- 20 J/cm2 a permanent fluorescent spot limited to the vessel was observed for the laser pulses targeted on the vessels; for the laser pulses targeted on the skin a transient low fluorescence circular spot was observed. For this fluence range a selective photocoagulation of a vessel was performed. (iii) for fluences ranging from 190 +/- 20 J/cm2 to 300 +/- 20 J/cm2 persistent intense fluorescence spots were observed on both skin and vessels. This type of fluorescence was related to an overdosage. CONCLUSION: These results are in fair agreement with the data of the literature about liposomes and with the data we obtained in a previous study on a vascular model. This study demonstrates the interest of a laser-induced release of liposome-encapsulated dye for a real-time quantification of thermal damage. Such a method could be useful for laser photocoagulation in ophthalmology for indications such as choroidal neovessels where the production of a precise thermal damage is required.

L24 ANSWER 25 OF 42 MEDLINE DUPLICATE 20
ACCESSION NUMBER: 96261574 MEDLINE
DOCUMENT NUMBER: 96261574 PubMed ID: 8778522
TITLE: Fluorescence measurement of 805 nm laser-induced release of 5,6-CF from DSPC liposomes for real-time monitoring of temperature: an in vivo study in rat liver using ***indocyanine*** ***green*** potentiation.
AUTHOR: Mordon S; Desmettre T; Devoisselle J M; Soulie S
CORPORATE SOURCE: INSERM U. 279, I.T.M., Pavillon Vancostenobel, Lille, France.
SOURCE: LASERS IN SURGERY AND MEDICINE, (1996) 18 (3) 265-70. Journal code: 8007168. ISSN: 0196-8092.
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AB BACKGROUND AND OBJECTIVE: This in vivo study examines the validity of using fluorescence measurements of laser-induced release of temperature-sensitive, liposome-encapsulated dye for real-time monitoring of temperature and for prediction of tissue thermal damage. STUDY DESIGN/MATERIALS AND METHODS: An in vivo study is performed in rat liver after i.v. injection of liposomes loaded with a fluorescent dye and i.v. injection of ***indocyanine*** ***green*** (***ICG***) for diode laser potentiation. Temperature-sensitive liposomes (DSPC: Di-Stearoyl-Phosphatidyl-Choline) are loaded with 5,6-carboxyfluorescein (5,6-CF). These liposomes (1.5 ml solution) and ***ICG*** (1.5 ml solution-5mg/kg) are injected in adult male wistar rats. Two hours later, the liver is exposed and irradiated with a 0.8 W diode laser using pulses lasting from 1-6s (fluence ranging from 16-98 J/cm2). Simultaneously, the fluorescence emission is analysed with an ultrahigh sensitivity intensified camera. RESULTS: The ***fluorescence*** ***intensity*** I(F) increases linearly from 18 J/cm2 up to 75 J/cm2. These fluences correspond to surface temperatures between 42 degrees C and 65 degrees C. The measurements appear to be highly reproducible. In this temperature range, the accuracy is +/- 3 degrees C. The maximum intensity is observed immediately after the laser is switched off. A decrease of the ***fluorescence*** ***intensity*** (27% in 20 minutes) is observed due to the 5,6-CF clearance. However, the ratio I(F)/I(BCK) (I(BCK): background ***fluorescence*** ***intensity***) remains almost stable over this period of time and the determination of the temperature is still possible with good accuracy even 20 minutes after laser irradiation. CONCLUSION: Real-time temperature monitoring by using

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Microvascular Research 55, 146–152 (1998)
Article No. MR982068

Indocyanine Green: Physicochemical Factors Affecting Its Fluorescence *in Vivo*

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This study reinvestigates the spectral properties of ICG (Indocyanine green) *in vivo*, the role of quenching, and the possibility of an interaction of ICG with blood components and/or vessel walls. ICG quenching as a function of concentration was studied by spectrophotometry on whole blood samples from golden hamsters. Fluorescence ICG characteristics were evaluated by front-face fluorometry. *In vivo*, fluorescence measurements were performed on the femoral artery of golden hamsters. *In vitro*, on whole blood samples, fluorescence intensity is modified by ICG quenching as concentration increases above 80 μg/ml. The maximum fluorescence peak is not affected and remains centered at 832 nm. The *in vivo* measurements display a similar fluorescence intensity shape, which is affected only by ICG concentrations. However, the maximum fluorescence emission peak is modified significantly with time. Between 0 and 120 min, four phases can be distinguished in which a wavelength shift from 826 to 835 nm is observed. The wavelength shift with change in fluorescence intensity observed *in vivo* could be due to a localization of ICG molecules in sites more hydrophobic than serum proteins. It is possible to hypothesize the presence of an endothelium-bound form with a specific fluorescence spectrum. The amphiphilic properties of ICG are consistent with fixation of some ICG molecules on sites other than plasmatic proteins after injection. The process of fixation of ICG molecules on surface components or within the vascular endothelium could be due to a change in the microenvironment of some ICG molecules.

Key Words: indocyanine green; fluorescence; proteins; blood; quenching.

INTRODUCTION

Fluorescein angiography is an established and important diagnostic method in ophthalmology and in capillary microscopy for the study of several human microangiopathies (Bollinger *et al.*, 1991). In gastroenterology, this method has been proposed for studying blood vessels of the stomach, the intestine, and the colon since tissue perfusion plays an important role in several diseases. For example, progressive reduction in neoterminal ilea blood flow after ileocolonic resection for Crohn's disease may accompany recurrence of this disease (Angerson *et al.*, 1993). Our group has already proposed a fluorescence endoscopic imaging technique using fluorescein sodium to study the anastomotic recurrence of Crohn's disease (Maunoury *et al.*, 1996). In that study, we showed that blood flow was increased in early-stage disease and reduced in late-stage disease

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while the submucosal fibrosis involved the small vessels. However, this endoscopic fluorescence imaging technique did not reflect blood flow throughout the full thickness of the bowel wall. Endoscopic fluorescence imaging using fluorescein could miss a reduction in flow in the deeper layers of the bowel wall, which may be the main site of vascular compromise.

Using a fluorescent molecule with an absorption peak in the infrared spectrum, such as indocyanine green (ICG), could provide a means of imaging deeper layers of the bowel wall. ICG is a relatively large molecule (MW 775) and is known to bind to plasma proteins such as albumin, globulins, and lipoproteins. These characteristics increase intravascular ICG dye retention compared with sodium fluorescein. However, most data related to the kinetics of ICG dye were established on the basis of angiographic observation from absorption ICG angiography (Flower and Hocheimer, 1977). It is usually stated that the half-life of ICG in blood is about 3–4 min. However, Hollins *et al.* (1987) and Ott *et al.* (1994) have shown that after a bolus injection, plasmatic concentration of ICG follows a biexponential decay.

One report states that the concentration of the ICG solution and the nature of the solvent have a significant influence on the absorption properties of ICG molecules (Zhou *et al.*, 1994). Immediately after intravenous injection, binding to the plasmatic proteins induces a shift in the maximum of the absorption spectra from 780 to 805 nm (Landsman *et al.*, 1976; Flower, 1995). This shift corresponds to the conversion of an aqueous solution of ICG (i.e., aggregated ICG as oligomers) to a whole blood solution of ICG (i.e., ICG bound to the plasmatic proteins). Our research group has demonstrated that *in vitro* ICG is able to interact with surfactant micelles or the phospholipid bilayer and the emission peak can be shifted toward 830 nm (Devoisselle *et al.*, in press).

The shape of the absorption spectrum changes with ICG concentration as the proportion of aggregated molecules increases. Plasmatic proteins interact with the aggregation process because they bind preferentially to the nonaggregated ICG molecules. In that way, plasmatic proteins reduce the aggregation process. The interaction of the two processes, aggregation and binding to the plasmatic protein, contributes to the relative stability of the ICG absorption spectra in whole blood solution after the initial dilution (Zhou *et al.*, 1994). However, there are only a few reports about the interactions of ICG with blood vessel walls. Although many authors mention a more or less selective fixation of ICG on the vessel wall of CNV (choroidal neovascularization) compared to normal choroidal vessels (Flower, 1995; Devoisselle *et al.*, 1997; Guyer *et al.*, 1992) in ophthalmology, this selectivity remains to be proven (Flower, 1994; Destro and Puliafito, 1989; Scheider *et al.*, 1992). Leakage is a mechanism proposed in an ocular pathology (Ho *et al.*, 1994) or perhaps ICG leaves the blood compartment when bound to albumin (Klingbeil *et al.*, 1995).

Since little is currently known about the spectral and fluorescence behavior of ICG *in vivo*, we were interested in comparing the quenching effects induced by high ICG concentrations *in vitro* and *in vivo* and describing the fluorescence spectral modifications occurring *in vivo* in a blood vessel.

MATERIALS AND METHODS

Animals

Male golden hamsters (n = 12) with an average weight of 100 g were anesthetized with an intramuscular injection of a combination of ketamine (150 mg/kg; Imalgène 500, Rhône Mérieux, France) and chlorpromazine (0.50 mg/kg; Largactil, Spécia Rhône Poulenc Rorer, France). For each hamster, blood samples were taken and fluorescence was measured on the femoral artery. Bolus injections of the ICG solution (3 or 15 mg/kg) were performed through the tongue vein. One animal was killed and the blood collected in order to perform ICG dilution in whole blood. The experimental procedures used conformed to the Ministère de l'Agriculture et de la Pêche Resolution on the use of animals in research and to the guiding principles of the American Physiological Society.

ICG

Infracyanine (SERB, France), a recently synthesized ICG preparation without β-naphthylamine nor any iodide component, was used. ICG was reconstituted with sterile water immediately before use. To study ICG quenching in blood *in vitro*, the ICG concentration

range was 0.001 to 1 mg/ml. *In vivo*, two different concentrations were used in this study, corresponding to 3 and 15 mg/kg. The concentration of 15 mg/kg (360 μg/ml) was chosen to study the behavior of a high local concentration of the dye in blood vessels. The concentration of 3 mg/kg (70 μg/ml) was used as a reference since this concentration was too low to obtain a fluorescence quenching.

ICG Quenching in Blood in Vitro

For determination of IGC quenching properties *in vitro*, ICG was dissolved in water and diluted to appropriate concentrations in plasma and whole blood (collected in heparinized tubes). In order to minimize dilution errors, a high-concentration ICG solution was prepared (20 mg/ml) and immediately diluted in whole blood. The concentration range was 0.001 to 1 mg/ml. All solutions were protected from light and used immediately after preparation. Samples were placed in a cuvette (100-μm optical path length) and the reference cuvette was filled with whole blood.

ICG Characteristics in Blood in Vivo

ICG was administered to anesthetized hamsters by intravenous injection at two different doses (3 and 15 mg/kg body wt). Immediately after injection of ICG, blood samples were taken from the ophthalmic venous plexus using the retro-orbital bleeding technique (Riley, 1960) with 20-μl-heparinized capillary tubes (Microcapps, Hemocapps heparinized; Drummond Scientific Co.). In this way, a minimal blood volume can be collected and several samplings can be performed. The whole blood was immediately placed in a 100-μm cuvette and absorption and fluorescence characteristics were studied. For these studies a reference cuvette, filled with whole blood, was used. Fluorescence spectra were recorded from 750 to 900 nm at a 720-nm excitation wavelength (RF-5000 spectrofluorometer, Shimadzu, Japan, equipped with an RP-928 extended photomultiplier, Hamamatsu, Japan). Due to the presence of high scattering media, front-face fluorometry was chosen instead of a 90° angle measurement (Eisinger and Flores, 1979). The cuvette was placed at a 54° to 36° angle to minimize the reflection of the excitation light. ICG was excited at 720 nm in order to have sufficient light energy and a large wavelength range between excitation and emission. Half-band widths were fixed at 10 nm (excitation) and 15 nm (emission).

For determination of the ICG clearance in plasma and using the same blood sampling procedure, the blood was diluted 20-fold in an isotonic glucose solution and centrifuged (3000 rpm, 5 min, Sigma 113, USA) for optimal optical density measurements. The supernatant was placed in a cuvette (1-cm path length) and absorption was measured at 805 nm (Uvikon 922 spectrophotometer; Kontron, Germany) with diluted plasma from the same animal before dye injection as reference. ICG concentration in plasma was calculated on the basis of a calibration curve of ICG in diluted plasma. As ICG is cleared from the circulation in a biphasic exponential decay pattern, experimental data were processed by nonlinear regression (MINIM software, 39 data points, Hartley's interpolation, 5 iterations).

In Vivo Fluorescence Measurement

Fluorescence intensity and fluorescence emission spectra were recorded with a spectrofluorometer. A filtered 150-W xenon lamp was used for fluorescence excitation (Model 66056; ORIEL Corp., Stratford, CT). The excitation wavelength was selected using a narrow band interference filter (FWHM = 40 nm) centered at 720 nm, corresponding to the absorption maxima range of ICG. The excitation light was then focused onto one branch of a bifurcated silica optical fiber bundle (Sedi, France) of 0.5-mm diameter. Using this setup, the excitation power density delivered to the target was 5 mW/cm^2. The tissue fluorescence was transmitted by the second branch of the optical fiber bundle, focused into a spectrograph (CP 200; Jobin Yvon, France), spectrally dispersed, and imaged onto an optical multichannel analyzer (MISA; Jobin Yvon, France). The fluorescence was detected in the wavelength range 500 to 850 nm. The fluorescence spectrum was digitized and the data were stored and analyzed using a microcomputer and specific software (Spectraview-2D, Jobin-Yvon Instruments).

Measurements were performed on the femoral artery, since the optical fiber of the spectrofluorometer required a recording surface of 0.5 mm in diameter. Before injection, autofluorescence was studied. As soon as ICG was injected, 15 spectra were recorded within the first 5 min and 15 spectra were recorded until 120

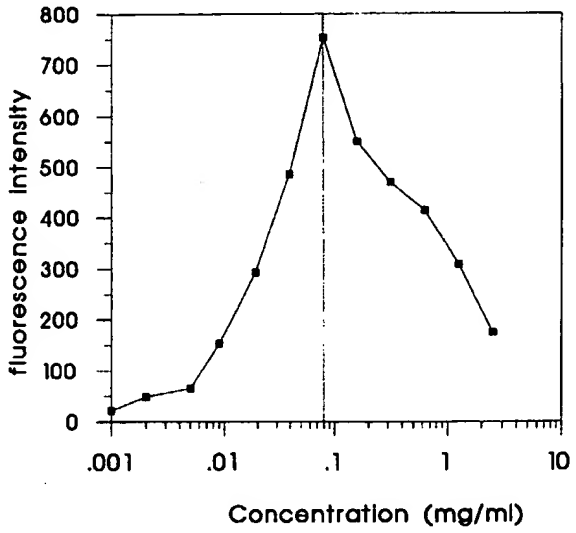

FIG. 1. Fluorescence intensity of ICG in whole blood (golden hamster) as a function of ICG concentration. Fluorescence is maximum at 80 μg/ml (quenching threshold).

min after the ICG injection. Fluorescence intensities and maximum fluorescence peak wavelength (λ_{max}) were studied as a function of time.

Data Evaluation

Except for the kinetics of ICG elimination from blood (nonlinear regression as described previously), plotted data are the medians and standard error of the medians.

RESULTS

Figure 1 shows the relative fluorescence intensity of ICG in whole blood *in vitro* as a function of ICG concentration. The maximum fluorescence intensity is observed at 80 μg/ml. At higher concentrations, the fluorescence intensity decreases nonlinearly. Spectroscopic analysis shows that the peak of maximum fluorescence intensity (λ_{max}) remains stable at 832 nm, whatever the concentration.

The kinetic profile of ICG concentration in total blood samples obtained *in vivo* is shown in Fig. 2. Using these data and a nonlinear regression, interpolation confirms that the ICG blood clearance is biphasic.

The equation is $[ICG]_{blood}(t) = C \cdot [A \exp(-k_1 \cdot t) + B \exp(-k_2 \cdot t)]$, with $k_1 = 0.014 \pm 008\ min^{-1}$, $k_2 = 0.097 \pm 0.015\ min^{-1}$, $A = 1.54 \pm 0.82$, $B = 7.75 \pm 0.72$, and $C = 40$.

Using this equation and taking 80 μl/ml as the threshold value (ICG quenching threshold), it is possible to calculate that ICG quenching in blood should last approximately 23 min when ICG is injected at $t = 0$ at a dose of 360 μg/ml (15 mg/kg administered dose).

The fluorescence kinetic profiles of total blood samples are shown in Fig. 3. ICG is administered to hamsters at two different doses: (i) 15 mg/kg corresponding to 360 μg/ml and (ii) 3 mg/kg corresponding to 70 μg/ml (below the quenching threshold).

Clearance of ICG administered at 3 mg/kg shows a continuous elimination profile until the end of the experiment. When ICG is administered at 15 mg/kg, ICG fluorescence is quite different; a rapid increase followed immediately by a rapid decrease is observed in the first 5 min. These two phases are followed by a slower increase, reaching a plateau at approximately 20 min. The late phase consists of a slow decrease in the fluorescence intensity. For both dosage forms, spectroscopic analysis shows that the peak of maximum intensity (λ_{max}) remains stable at 832 nm during the entire experiment.

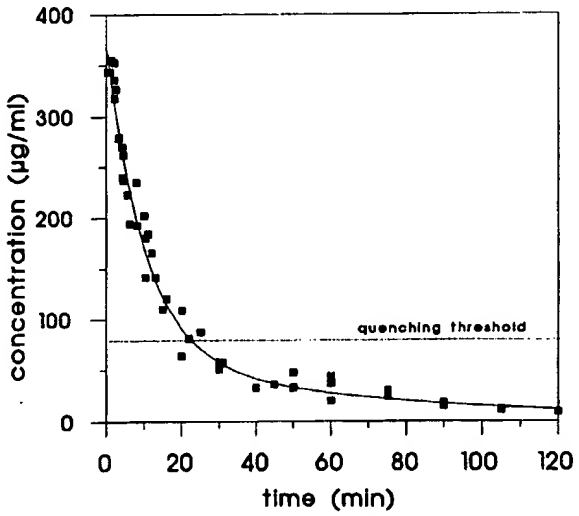

FIG. 2. Absorption kinetic profile of ICG in whole blood as a function time. Blood samples were taken from the ophthalmic plexus of golden hamsters ($n = 3$). The dotted line corresponds to the ICG quenching threshold in whole blood.

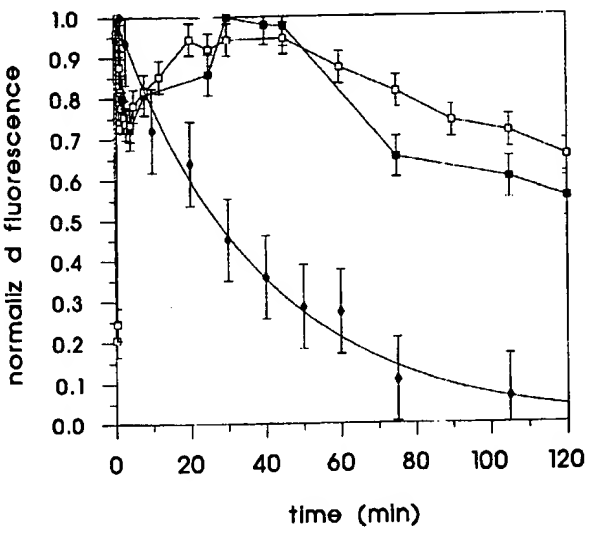

FIG. 3. Fluorescence kinetic profile of ICG in whole blood as a function of time. Blood samples were taken from the ophthalmic plexus after injection of 3 mg/kg (♦) or 15 mg/kg (■). Fluorescence kinetic profile of ICG recorded on the femoral artery *in vivo*, after previous injection of ICG at 15 mg/kg (360 μg/ml) (□). Each value is the mean of measurements performed on three different animals (excitation, 720 nm).

Figure 3 also displays the fluorescence kinetic profile recorded on the vessel after injection of a 15 mg/kg dose. This kinetic profile obtained *in vivo* is quite similar to that obtained *in vitro* for total blood samples for the same dosage. Similarly, when ICG is administered at 3 mg/kg, a continuous elimination profile is obtained, similar to that obtained for total blood samples (data not shown).

However, when the fluorescence is recorded on the vessel wall, the peak of maximum intensity does not remain stable (Fig. 4). The peak of maximum intensity is initially at 826 ± 1 nm. Within the first 2 min after injection, λ_{max} rapidly increases to 835 ± 1 nm to reach its maximum. Then, λ_{max} stays stable at 834 ± 1 nm for approximately 20 min. The late λ_{max} phase consists of a slow decrease toward the initial value of 826 ± 1 nm.

DISCUSSION

Fluorescence and absorption characteristics of ICG in aqueous solution are well documented (Zhou *et al.*, 1994) but only a few studies refer to these properties in biological media (Devoisselle *et al.*, 1997). ICG quenching in blood was studied by performing blood sampling and *in vitro* measurements on whole blood (no dilution). ICG quenching in whole blood is obtained at concentrations of 80 μg/ml and above. This value is in accordance with those reported in the literature (Baker, 1966; Benson and Kues, 1978). Interestingly, the ICG fluorescence intensity curve as a function of ICG concentration has an asymmetric shape (Fig. 1). As observed by Benson and Kues (1978) and Van den Biesen *et al.* (1995), the increase in ICG concentration resulted in a nonlinear decrease of the fluorescence intensity. The quenched part displays fluorescent intensities higher than those in the nonquenched part of the curve (0.001 to 0.08 mg/ml). As pointed out by Van den Biesen *et al.* (1995), the near-infrared light can be diffused by red blood cells, leading to an increase in the fluorescence intensity. The main explanation is probably that the same amount of ICG per unit of volume results in a higher fluorescence intensity because dye is excluded from red blood cells and is concentrated in plasma. The influence of shear on the yield of fluorescence was described by Van den Biesen *et al.* (1995). In our study, all measurements were performed on blood in stasis. However, as demonstrated by Van den Biesen *et al.* (1995), below a 100-μm layer thickness,

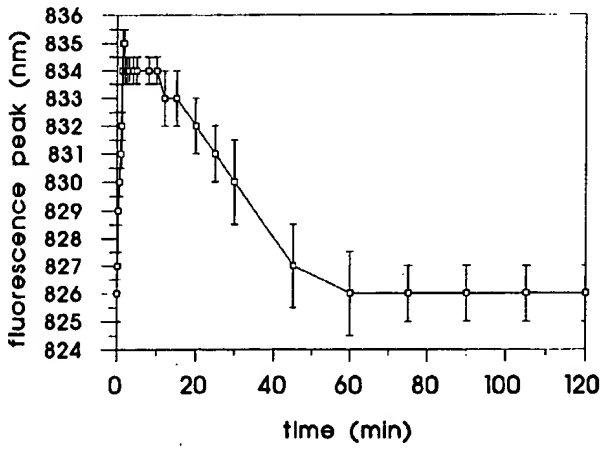

FIG. 4. Evolution of the maximum fluorescence peak wavelength (λ_{max}) as a function of time (excitation, 720 nm). The fluorescence was recorded on the femoral artery *in vivo* after previous injection of ICG at 3 (n = 3) or 15 mg/kg (n = 3). Each value is the mean of measurements performed on six different animals.

the yield of fluorescence is similar for flowing blood and blood in stasis.

We used the kinetic concentration profiles of total blood samples in our study to determine the exact concentration of ICG in blood as a function of time. The two injected doses were chosen as follows: (i) 15 mg/kg to evaluate the role of quenching on fluorescence intensity and on the spectral emission; (ii) 3 mg/kg to avoid ICG quenching. Consequently, it was possible to study the influence of quenching and to compare data obtained in blood samples and *in vivo* on a femoral artery.

As a consequence, the fluorescence kinetic profile obtained for 15 mg/kg does not follow the conventional clearance. A few seconds after injection, elimination of ICG by the liver begins and the ICG concentration decreases until it reaches the dequenching concentration. However, at 15 mg/kg (corresponding to 360 μg/ml in our study), the concentration is so high that quenching occurs again. Figure 3 shows that quenching is observed up to approximately 25 min, which is in accordance with the data obtained by calculation (23 min). This duration allows ICG concentration in whole blood to decrease to 80 μg/ml. Between 25 and 40 min, the fluorescence intensity remains almost constant because elimination is compensated for by the dequenching of the ICG fluorescence. The role of quenching of the fluorescence emission is clearly demonstrated when a 15 mg/kg dose is used.

At 3 mg/kg (corresponding to 70 μg/ml), the concentration is below that required for ICG quenching in whole blood. Consequently, clearance follows a conventional clearance curve. The calculation, the fluorescence observed in blood samples, and the fluorescence observed on the femoral artery are in accordance.

The maximum fluorescence peak wavelength recorded on whole blood samples at 3 or 15 mg/kg remains stable at 832 nm during the entire experiment. When the fluorescence is recorded on the vessel wall, a shift in the peak is observed (Fig. 4). Four phases can be distinguished between 825 and 835 nm. Since it was observed with and without quenching, this shift cannot be related to the dose. This phenomenon can be explained.

(i) Binding of ICG to the blood components. It has been reported that ICG aggregates in aqueous solution but binds to proteins, limiting this aggregation property in plasma and blood (Landsman *et al.*, 1976). The maximum emission peak of ICG in albumin solution differs from that in plasma or blood, confirming the ability of ICG to bind to structures other than proteins such as lipoproteins. Similarly, ICG is able to interact with surfactant micelles or the phospholipid bilayer with quenching, fluorescence enhancement, and wavelength shift, depending on the nature of the interface (Devoisselle *et al.*, 1997). Probably the hydrophobic part of ICG (heterocycles) is partly embedded in the hydrophobic core of proteins or in the outer layer of lipoproteins. Another type of interaction with unknown amphiphatic molecules or structures and an aggregation process due to the ICG binding cannot be excluded. All binding sites could be saturated above a given concentration. ICG would then not be aggregated and the quenching could be due to dye–protein interactions or possibly dye–dye interactions. However, no data concerning the binding properties of ICG to plasmatic components are currently available. Previous studies have shown that new absorption peaks appear only at concentrations above 2.5 mg/ml, indicating self-aggregation of the dye. However, in our study, the shift was observed on the vessel wall at concentrations below 2.5 mg/ml, suggesting that interaction with lipoproteins is the main mechanism.

(ii) Binding of ICG at the endothelium or cellular level. The change in maximum emission wavelength with time could be explained by changes in the microenvironment of the dye. These modifications indicate that components other than those already described interact with ICG. These other components could be either the endothelial wall or white cells such as leukocytes.

With regard to the endothelial wall, ICG could bind to the cell coat or penetrate into these cells. It has been demonstrated that ICG is able to diffuse across cell membranes. Intracellular uptake was observed when ICG was incubated with keratinocytes or colonic cancer cells (Fickweiler *et al.*, 1997; Baümler *et al.*, 1997). Moreover, fluorescence labeling of microvasculature is observed by visualization of fluorescence dots, which are the consequence of the labeling of leukocytes by ICG after a 30-min injection of ICG (Matsuada *et al.*, 1996).

In conclusion, the variation of the ICG emission peak *in vivo* clearly indicates that dye–protein interactions take place since no modification occurred in whole blood. This effect is of interest with regard to new applications of fluorescence angiography. The wavelength shift observed *in vivo* with a change in fluorescence

intensity could be due to a localization of ICG molecules at sites more hydrophobic than serum proteins. It is possible to hypothesize the presence of an endothelium-bound form with a specific fluorescence spectrum. The amphiphilic properties of ICG are consistent with binding of some ICG molecules on sites other than plasmatic proteins after injection. The process of binding of ICG molecules on proteins or more hydrophobic sites of the vascular endothelium could be due to a change in the polarity of the microenvironment of some ICG molecules.

ACKNOWLEDGMENTS

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L24 ANSWER 1 OF 42 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002338427 MEDLINE
DOCUMENT NUMBER: 22051100 PubMed ID: 12055464
TITLE: The ultra-late phase of ***indocyanine*** ***green*** angiography for healthy subjects and patients with age-related macular degeneration.
AUTHOR: Mori Keisuke; Gehlbach Peter L; Nishiyama Yoko; Deguchi Tatsuya; Yoneya Shin
CORPORATE SOURCE: Department of Ophthalmology, Saitama Medical School, Saitama, Japan.. keisuke@saitama-med.ac.jp
SOURCE: RETINA, (2002 Jun) 22 (3) 309-16.
Journal code: 8309919. ISSN: 0275-004X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020626
Last Updated on STN: 20020814
Entered Medline: 20020813
AB PURPOSE: To compare the characteristics of residual fundus fluorescence observed in the ultra-late phase of ***indocyanine*** ***green*** (***ICG***) angiography, in normal subjects and in patients with age-related macular degeneration (ARMD). METHODS: ***ICG*** angiography was performed on 38 patients, 21 had ARMD, 9 were normal subjects aged >62, and 8 were normal subjects aged <36. The ***intensity*** and pattern of ***fluorescence*** from angiograms obtained in the ultra-late phase, 24 hours after dye injection, was also recorded and analyzed. RESULTS: In the ultra-late phase, 95% of ARMD eyes with CNV showed geographic hypofluorescent lesions. All of the CNV that could be delineated with fluorescein and/or ***ICG*** angiography were located in these geographic lesions. In 73% of ARMD eyes without CNV, these hypofluorescent lesions occurred, while age-matched normal subjects had no hypofluorescent lesions. The mean ***intensity*** of ***fluorescence*** in the normal older subject group was significantly higher than that seen in the normal young subject group. CONCLUSIONS: Increased fluorescence, associated with older subjects, in the ultra-late phase of ***ICG*** angiography may reflect aging changes in the chorioretinal complex. Geographic hypofluorescent areas, demonstrated only in the ultra-late phase, associate with ARMD and may represent areas predisposed to CNV development.

L24 ANSWER 2 OF 42 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2002242140 MEDLINE
DOCUMENT NUMBER: 21976362 PubMed ID: 11979982
TITLE: Quantitative analysis of ***indocyanine*** ***green*** angiography in multifocal posterior pigment epitheliopathy and its related diseases.
AUTHOR: Sano Akemi; Mori Keisuke; Deguchi Tatsuya; Yoneya Shin
CORPORATE SOURCE: Department of Ophthalmology, Saitama Medical School, 38 Morohongo, Moroyama-machi, Iruma-gun, Saitama 350-0495, Japan.
SOURCE: NIPPON GANKA GAKKAI ZASSHI. ACTA SOCIETATIS OPHTHALMOLOGICAE JAPONICAE, (2002 Apr) 106 (4) 221-8.
Journal code: 7505716. ISSN: 0029-0203.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020501
Last Updated on STN: 20020614
Entered Medline: 20020613
AB PURPOSE: To clarify the ***indocyanine*** ***green*** (***ICG***) angiographic features in multifocal posterior pigment epitheliopathy(MPPE), we measured the maximum diameter of the choroidal vein and mean ***fluorescence*** ***intensity*** within the

vascular arcade. METHODS: ***ICG*** angiography was performed in 40 eyes of 20 patients with MPPE and 10 age-matched normal controls, and quantified by IMAGEnet. RESULTS: The mean maximum choroidal venous diameter was 544 +/- 162(mean +/- standard deviation) microns in eyes with MPPE and 278 +/- 55 microns in healthy age-matched control eyes. The mean ***fluorescence*** ***intensity*** was 106.9 +/- 52.5 and 86.5 +/- 32.5, respectively. Both the mean maximum choroidal venous diameter and the mean ***fluorescence*** ***intensity*** showed statistical difference between the two groups. In contrast, there was no statistically significant difference between the eyes with serous retinal detachment and without detachment in the MPPE group. CONCLUSIONS: These results show that choroidal venous dilation and choroidal hyperfluorescence in MPPE are clearly distinguished from choroidal aging changes. Additionally, these pathological angiographic changes seemingly do not delineate the activity of MPPE, but demonstrate the background factor of the pathogenesis of MPPE.

L24 ANSWER 3 OF 42 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2002087190 MEDLINE
DOCUMENT NUMBER: 21673491 PubMed ID: 11815349
TITLE: Choroidal perfusion perturbations in non-neovascular age related macular degeneration.
AUTHOR: Ciulla Thomas A; Harris Alon; Kagemann Larry; Danis Ronald P; Pratt Linda M; Chung Hak S; Weinberger Dov; Garzozi Hanna J
CORPORATE SOURCE: Department of Ophthalmology, Indiana University School of Medicine, Indianapolis, USA.
CONTRACT NUMBER: EY10801 (NEI)
SOURCE: BRITISH JOURNAL OF OPHTHALMOLOGY, (2002 Feb) 86 (2) 209-13. Journal code: 0421041. ISSN: 0007-1161.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020130
Last Updated on STN: 20020308
Entered Medline: 20020307
AB AIM: Choroidal perfusion, affected in age related macular degeneration (AMD), is difficult to objectively assess given the overlying retinal circulation. This study more objectively compared choroidal perfusion parameters in a group with non-neovascular AMD to an unaffected age matched control group. METHODS: 21 non-neovascular AMD subjects and 21 age matched control subjects without evidence of AMD underwent assessment of their choroidal blood flow in a case-control study. Scanning laser ophthalmoscope ***indocyanine*** ***green*** (***ICG***) angiograms were analysed by a new area dilution analysis technique. Four areas in the perifoveal region and two areas in the temporal peripapillary retina were evaluated by producing a graph of ***intensity*** of ***fluorescence*** of each area over time. The mean of the filling times and the heterogeneity of the filling times were assessed. RESULTS: The means of the filling times within the perifoveal regions and the hetereogeneity of the filling times between regions within the same eyes were significantly greater in the AMD patients compared with the control subjects. CONCLUSIONS: Delayed and heterogeneous filling of the choroid was objectively demonstrated in eyes with non-neovascular AMD compared with age matched controls without evidence of AMD, using an area dilution analysis technique applied to ***ICG*** angiography.

L24 ANSWER 4 OF 42 MEDLINE
ACCESSION NUMBER: 2002136507 MEDLINE
DOCUMENT NUMBER: 21860726 PubMed ID: 11871080
TITLE: [Changes in neovascular membranes and normal choroid blood vessels after multiple photodynamic therapy treatments]. Veranderungen neovaskularer Membranen und normaler Aderhautgefasse nach mehrfacher photodynamischer Therapie.
AUTHOR: Michels S; Barbazetto I; Schmidt-Erfurth U

CORPORATE SOURCE: Universitatsaugenklinik Lubeck, Ratzeburger Allee 160, 23538 Lubeck.. stephanmichels@hotmail.com
SOURCE: OPHTHALMOLOGE, (2002 Feb) 99 (2) 96-100.
Journal code: 9206148. ISSN: 0941-293X.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020302
Last Updated on STN: 20020501
Entered Medline: 20020430
AB PURPOSE: ***ICG*** angiography (ICGA) was used to document the effect of repeated PDT (verteporfin) on size and leakage of choroidal neovascularisation in age-related macular degeneration (AMD) and treatment-related side effects on the choroid. METHODS: Forty-two patients were followed over 24 months in a clinical trial for PDT in AMD. The ICGAs were performed every 3 months with a confocal laser scanning system. Patients received repeated verteporfin treatment. At each control visit, the patients were retreated if leakage was present in fluorescein angiography (FA). RESULTS: A continuous, highly significant reduction in CNV size and leakage area was found over 24 months. The initial CNV size dropped by 23% from 3.86 mm2 to 2.98 mm2. The leakage area in the late phase of the angiogram decreased by 30.3% from 5.0 mm2 to 3.5 mm2. A significant side effect of PDT on the choroid was documented by an increased hypofluorescent area in ICGA. The maximum size of the hypofluorescent area was reached after 12 months. At month 24, the choroidal fluorescence showed recovery in respect to area and ***intensity*** of ***fluorescence*** . But hypofluorescence surrounding the CNV lesion was already present in 40 out of 42 eyes before treatment. CONCLUSION: The ICGA confirms that repeated PDT treatments lead to a significant reduction in CNV size and leakage area over as long as 2 years. CNV lesions are surrounded by choriocapillary hypofluorescence in ICGA. PDT causes further hypoperfusion of the choroid but in the long-term significant recovery of choroidal perfusion was shown.

L24 ANSWER 5 OF 42 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001360594 MEDLINE
DOCUMENT NUMBER: 21314599 PubMed ID: 11421013
TITLE: Aging changes of the choroidal dye filling pattern in ***indocyanine*** ***green*** angiography of normal subjects.
AUTHOR: Ito Y N; Mori K; Young-Duvall J; Yoneya S
CORPORATE SOURCE: Department of Ophthalmology, Saitama Medical School, 38 Morohongo, Moroyama, Iruma-gun, Saitama 350-0495, Japan.. nisiyama@saitama-med.ac.jp
SOURCE: RETINA, (2001) 21 (3) 237-42.
Journal code: 8309919. ISSN: 0275-004X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20011029
Last Updated on STN: 20011029
Entered Medline: 20011025
AB PURPOSE: To study the aging changes in the choroid of healthy volunteers with ***indocyanine*** ***green*** (***ICG***) angiography. METHODS: Video ***ICG*** angiography with adjunctive computer-assisted image analysis was performed on 35 eyes of 30 healthy volunteers (age range, 21-81 years; mean +/- standard deviation, 50.5 +/- 16.2 years) to observe the aging changes of the choroid. RESULTS: In patients in the second and third decades of life, the subfoveal choroidal arterioles fluoresced initially with subsequent rapid filling of the feeding arterioles and choriocapillaris. The watershed zone was clearly observed. In patients older than age 50, the choroidal vasculature filled more slowly. Eventually, the margin of the watershed zone became blurred. The

quantitative analysis showed that the number of choroidal arterioles and the ***fluorescent*** ***intensity*** in the macular region were reduced with age ($P < 0.005$). In the early venous phase, hypofluorescent patches seen in all ages increased in size and number and remained with aging. The mean ***fluorescence*** ***intensity*** was not correlated statistically with age. CONCLUSIONS: The features of normal aging patterns of the choroid that we investigated are essential to the interpretation of ***ICG*** angiography and may help in understanding the physiologic and pathologic conditions of the choroidal circulations and the choroid and retina themselves.

L24 ANSWER 6 OF 42 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2002083321 MEDLINE
DOCUMENT NUMBER: 21668622 PubMed ID: 11809374
TITLE: Fluorescence of ***indocyanine*** ***green*** in blood: intensity dependence on concentration and stabilization with sodium polyaspartate.
AUTHOR: Maarek J M; Holschneider D P; Harimoto J
CORPORATE SOURCE: Department of Biomedical Engineering, University of Southern California, OHE 500, University Park, Los Angeles, CA 90089-1451, USA.. jmaarek@bmsrs.usc.edu
CONTRACT NUMBER: R01 MH NS62148 (NIMH)
SOURCE: JOURNAL OF PHOTOCHEMISTRY AND PHOTOBIOLOGY. B, BIOLOGY, (2001 Dec 31) 65 (2-3) 157-64.
Journal code: 8804966. ISSN: 1011-1344.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020128
Last Updated on STN: 20020528
Entered Medline: 20020522
AB ***Indocyanine*** ***green*** (***ICG***) has been widely used in cardiovascular, hepatic, and ophthalmologic studies. Application of this fluorescent dye has been handicapped by its poor stability in solution and by the complex dependence of its ***fluorescence*** ***intensity*** on concentration. Noncovalent interactions between ***ICG*** and sodium polyaspartate (PASP) stabilize ***ICG*** fluorescence in aqueous solution, but the effect of PASP on ***ICG*** fluorescence in blood has not been described. The current study had two main goals: first, to characterize in vitro in blood the relationship between ***fluorescence*** ***intensity*** and concentration of ***ICG*** -PASP (***ICG***) and the stability of this relationship over time; second, to test a new phenomenological model describing the dependence of ***ICG*** fluorescence on concentration. Freshly-prepared ***ICG*** and ***ICG*** -PASP solutions produced the same ***fluorescence*** ***intensity*** over a wide range of concentrations (0.0005-0.1271 mg/ml). The peak fluorescence of ***ICG*** was reduced by 11% after 10 h and by 72% at 7 days. In contrast, the peak ***fluorescence*** ***intensity*** of ***ICG*** -PASP solutions was nearly unchanged for up to 14 days. The dependence of the ***fluorescence*** ***intensity*** on concentration was accurately represented by our model that accounted for the generation of fluorescence following light absorption, and for the reabsorption of the emitted fluorescence by ***ICG*** .

L24 ANSWER 7 OF 42 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2001473511 MEDLINE
DOCUMENT NUMBER: 21217435 PubMed ID: 11321138
TITLE: Dynamic observation of selective accumulation of a photosensitizer and its photodynamic effects in rat experimental choroidal neovascularization.
AUTHOR: Hikichi T; Mori F; Nakajima S; Takamiya T A; Takeda M; Sasaki M; Horikawa Y; Yoshida A
CORPORATE SOURCE: Department of Ophthalmology, Asahikawa Medical College, Japan.. hikichi@asahikawa-med.ac.jp

SOURCE: RETINA, (2001) 21 (2) 126-31.
Journal code: 8309919. ISSN: 0275-004X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010827
Last Updated on STN: 20010827
Entered Medline: 20010823

AB PURPOSE: The authors investigated the selective accumulation of a photosensitizer, ATX-S10(Na), in experimental choroidal neovascularization (CNV) in rats using a highly sensitive colorchromatic charge coupled device (CCD) camera. METHODS: To detect the development of experimental CNV in 30 rats, the animals were followed weekly with simultaneous fluorescein and ***indocyanine*** ***green*** angiography. After injecting ATX-S10(Na), the authors detected fluorescence from the photosensitizer using a highly sensitive color CCD camera. The camera was connected to a surgical microscope, under which rat fundi were observed through a coverglass in contact with the cornea. The retinas were excited with 405-435 nm light, and the light emitted from the photosensitizer passed through a 680-nm bandpass filter before being detected by the CCD camera. RESULTS: Immediately after injection, fluorescence appeared in the retinal vessels and then the entire retina. Thirty minutes postinjection, the ***intensity*** of the ***fluorescence*** was still strong from the whole retina, and the CNV was not detected. One hour after injection, retinal fluorescence was weak but still observable; 1.5 hours postinjection, retinal fluorescence was undetectable but fluorescence was strong from the CNV. Under the optimum therapeutic conditions, CNV was effectively occluded. CONCLUSION: ATX-S10(Na) selectively accumulates in the CNV in rats. The optimum therapeutic timing is approximately 1.5 hours postinjection of the dye in this CNV model.

L24 ANSWER 8 OF 42 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000215349 EMBASE
TITLE: Comparative single-molecule and ensemble myosin enzymology: Sulfoindocyanine ATP and ADP derivatives.
AUTHOR: Oiwa K.; Eccleston J.F.; Anson M.; Kikumoto M.; Davis C.T.; Reid G.P.; Ferenczi M.A.; Corrie J.E.T.; Yamada A.; Nakayama H.; Trentham D.R.
CORPORATE SOURCE: Dr. D.R. Trentham, The Ridgeway, Natl. Institute for Medical Research, Mill Hill, London NW7 1AA, United Kingdom. dtrenth@nimr.mrc.ac.uk
SOURCE: Biophysical Journal, (2000) 78/6 (3048-3071).
Refs: 79
ISSN: 0006-3495 CODEN: BIOJAU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Single-molecule and macroscopic reactions of fluorescent nucleotides with myosin have been compared. The single-molecule studies serve as paradigms for enzyme-catalyzed reactions and ligand-receptor interactions analyzed as individual stochastic processes. Fluorescent nucleotides, called Cy3-EDA-ATP and Cy5-EDA-ATP, were derived by coupling the dyes Cy3.29.OH and Cy5.29.OH (compounds XI and XIV, respectively, in Mujumdar et al. (1993, Bioconjug. Chem. 4:105-111)) with 2'(3')-O-[N:(2-aminoethyl)carbamoyl]ATP (EDA-ATP). The ATP(ADP) analogs were separated into their respective 2'- and 3'-O-isomers, the interconversion rate of which was 30[OH-] s-1 (0.016 h- 1 at pH 7.1) at 22.degree.C. Macroscopic studies showed that 2'(3')-O-substituted nucleotides had properties similar to those of ATP and ADP in their interactions with myosin, actomyosin, and muscle fibers, although the ATP analogs did not relax muscle as well as ATP did. Significant differences in the ***fluorescence*** ***intensity*** of Cy3-nucleotide 2'- and 3,-O-isomers in free solution and when they interacted with myosin were

evident. Single-molecule studies using total internal reflection fluorescence microscopy showed that reciprocal mean lifetimes of the nucleotide analogs interacting with myosin filaments were one- to severalfold greater than predicted from macroscopic data. Kinetic and equilibrium data of nucleotide-(acto)myosin interactions derived from single-molecule microscopy now have a biochemical and physiological framework. This is important for single-molecule mechanical studies of motor proteins.

L24 ANSWER 9 OF 42 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 2000498848 MEDLINE
DOCUMENT NUMBER: 20433677 PubMed ID: 10979299
TITLE: Quantitative analysis of ***indocyanine*** ***green*** angiographic image in central serous chorioretinopathy.
AUTHOR: Nishiyama Y; Mori K; Murayama K; Yoneya S
CORPORATE SOURCE: Department of Ophthalmology, Saitama Medical School, Japan.
SOURCE: NIPPON GANKA GAKKAI ZASSHI. ACTA SOCIETATIS OPHTHALMOLOGICAE JAPONICAE, (2000 Aug) 104 (8) 577-83. Journal code: 7505716. ISSN: 0029-0203.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001027
Last Updated on STN: 20001027
Entered Medline: 20001019
AB PURPOSE: To disclose the possible involvement of choroidal vascular change in development of central serous chorioretinopathy (CSC). METHODS: ***Indocyanine*** ***green*** (***ICG***) angiography was performed in 31 eyes with acute CSC, and 21 eyes from normal subjects. The maximum diameter of the choroidal veins and ***intensity*** of background ***fluorescence*** in the posterior fundus with ***ICG*** video images were measured for further analysis using IMAGEnet (Topcon). Then the results from CSC affected eyes, their fellow eyes, and normal eyes were compared. Aging factors were taken into consideration when we analyzed the data. RESULT: The maximum diameters of the choroidal veins were larger in both affected and fellow eyes than in the normal eyes ($p < 0.001$), and had a positive correlation with aging particularly in fellow eyes ($r = 0.36$). Both in the affected and fellow eyes, the background ***fluorescein*** ***intensity*** in the posterior pole of the late phase images was lower than in the normal eyes ($p < 0.001$), and was correlated with aging ($r = 0.28$, $r = 0.43$). CONCLUSION: This quantitative study showed that choroidal venous dilatation and the residual background fluorescence in the posterior fundus might be positive findings reflecting the pathogenesis of CSC.

L24 ANSWER 10 OF 42 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 2000460427 MEDLINE
DOCUMENT NUMBER: 20369386 PubMed ID: 10911733
TITLE: Pharmacokinetics of ***ICG*** and HPPH-car for the detection of normal and tumor tissue using fluorescence, near-infrared reflectance imaging: a case study.
AUTHOR: Gurfinkel M; Thompson A B; Ralston W; Troy T L; Moore A L; Moore T A; Gust J D; Tatman D; Reynolds J S; Muggenburg B; Nikula K; Pandey R; Mayer R H; Hawrysz D J; Sevick-Muraca E M
CORPORATE SOURCE: School of Chemical Engineering, Purdue University, West Lafayette, IN, USA.
CONTRACT NUMBER: K04 CA68374 (NCI)
R01 CA67176 (NCI)
SOURCE: PHOTOCHEMISTRY AND PHOTOBIOLOGY, (2000 Jul) 72 (1) 94-102. Journal code: 0376425. ISSN: 0031-8655.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20001005
Last Updated on STN: 20001005
Entered Medline: 20000927

AB We present in vivo fluorescent, near-infrared (NIR), reflectance images of ***indocyanine*** ***green*** (***ICG***) and carotene-conjugated 2-devinyl-2-(1-hexyloxyethyl) pyropheophorbide (HPPH-car) to discriminate spontaneous canine adenocarcinoma from normal mammary tissue. Following intravenous administration of 1.0 mg kg-1 ***ICG*** or 0.3 mg kg-1 HPPH-car into the canine, a 25 mW, 778 nm or 70 mW, 660 nm laser diode beam, expanded by a diverging lens to approximately 4 cm in diameter, illuminated the surface of the mammary tissue. Successfully propagating to the tissue surface, ***ICG*** or HPPH-car fluorescence generated from within the tissue was collected by an image-intensified, charge-coupled device camera fitted with an 830 or 710 nm bandpass interference filter. Upon collecting time-dependent fluorescence images at the tissue surface overlying both normal and diseased tissue volumes, and fitting these images to a pharmacokinetic model describing the uptake (wash-in) and release (wash-out) of fluorescent dye, the pharmacokinetics of fluorescent dye was spatially determined. Mapping the ***fluorescence*** ***intensity*** owing to ***ICG*** indicates that the dye acts as a blood pool or blood persistent agent, for the model parameters show no difference in the ***ICG*** uptake rates between normal and diseased tissue regions. The wash-out of ***ICG*** was delayed for up to 72 h after intravenous injection in tissue volumes associated with disease, because ***ICG*** fluorescence was still detected in the diseased tissue 72 h after injection. In contrast, HPPH-car pharmacokinetics illustrated active uptake into diseased tissues, perhaps owing to the overexpression of LDL receptors associated with the malignant cells. HPPH-car fluorescence was not discernable after 24 h. This work illustrates the ability to monitor the pharmacokinetic delivery of NIR fluorescent dyes within tissue volumes as great as 0.5-1 cm from the tissue surface in order to differentiate normal from diseased tissue volumes on the basis of parameters obtained from the pharmacokinetic models.

L24 ANSWER 11 OF 42 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:260775 CAPLUS
DOCUMENT NUMBER: 130:278931
TITLE: Method and apparatus for fluorometric analysis of serum protein compositions
INVENTOR(S): Araki, Ryuichiro; Yamashita, Yutaka
PATENT ASSIGNEE(S): Hamamatsu Photonics K. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11108924	A2	19990423	JP 1997-269905	19971002

PRIORITY APPLN. INFO.: JP 1997-269905 19971002

AB A compn. of serum proteins is detd. by (1) adding fluorescence reagents, which are bound to proteins and show different fluorescence lifetime for each protein, to samples (serum, plasma, or blood), (2) irradiating the samples with excitation light, and (3) measuring the time-dependent change in the ***fluorescence*** ***intensity*** . An app. for the method is also claimed. LDL/HDL ratio in the serum of a healthy male volunteer was measured by using ***indocyanine*** ***green*** which shows binding const. to lipoproteins higher by 2 orders of magnitude compared with that to serum albumin, globulins, etc.

L24 ANSWER 12 OF 42 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 2000002075 MEDLINE

DOCUMENT NUMBER: 20002075 PubMed ID: 10381670
TITLE: Subtraction ***ICG*** angiography in Harada's disease.
AUTHOR: Kohno T; Miki T; Shiraki K; Kano K; Matsushita M; Hayashi K; De Laey J J
CORPORATE SOURCE: Department of Ophthalmology, Osaka City University Medical School, Japan.
SOURCE: BRITISH JOURNAL OF OPHTHALMOLOGY, (1999 Jul) 83 (7) 822-33.
Journal code: 0421041. ISSN: 0007-1161.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000124
Last Updated on STN: 20000124
Entered Medline: 20000110
AB BACKGROUND/AIM: The significance of ***indocyanine*** ***green*** (***ICG***) angiography (ICGA) in Harada's disease still awaits clarification in many respects. This study investigates the details of choroidal lesions observed in Harada's disease by the subtraction method. METHODS: Eight patients with Harada's disease were followed with ICGA. ***ICG*** angiograms were obtained with a Topcon high resolution digital fundus camera and processed with a Topcon IMAGEnet computer system. Image subtraction was conducted for analysing serial angiograms taken at about 2 second intervals during the dye transit phase and those taken in the early and middle phases of angiography. RESULTS: Standard ***ICG*** images of acute stage disease showed delayed choroidal filling in the early phase. Mid phase angiograms showed areas with bright ***fluorescence*** of variable ***intensity*** , indicating intrachoroidal ***ICG*** leakage. With image subtraction of angiograms with an interval of seconds the choroidal vessels could be imaged sequentially, with the choroidal arteries visualised first, followed by the definition of the choriocapillaris and then the choroidal veins. The choroidal veins with delayed filling were visualised as positive images in serial subtraction angiograms. Subtraction with an interval of minutes showed uneven background fluorescence and bright fluorescence corresponding to the areas of intrachoroidal ***ICG*** leakage. After the disease subsided with steroid therapy, angiography revealed an improvement in delayed choroidal filling. Image subtraction by the second allowed a clear visualisation of improved choroidal venous filling, while subtraction by the minute showed homogeneous background fluorescence, eliminating brighter areas. CONCLUSION: Subtraction ICGA demonstrated that delayed filling of the choroidal veins of varying severity occurs in association with hyperpermeability of the choroidal vessels in the course of Harada's disease.

L24 ANSWER 13 OF 42 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 2000107926 MEDLINE
DOCUMENT NUMBER: 20107926 PubMed ID: 10643314
TITLE: [Confocal ***indocyanine*** ***green*** angiography with 3-dimensional topography. Results in choroid neovascularization (CNV)].
Konfokale Indozyaningrun-Angiographie mit dreidimensionaler Topographie. Ergebnisse bei chorioidaler Neovaskularisation (CNV).
AUTHOR: Schmidt-Erfurth U; Noack J; Teschner S; Birngruber R
CORPORATE SOURCE: Augenklinik Universitat Lubeck.
SOURCE: OPHTHALMOLOGE, (1999 Dec) 96 (12) 797-804.
Journal code: 9206148. ISSN: 0941-293X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000314
Last Updated on STN: 20000314
Entered Medline: 20000229

AB BACKGROUND: Confocal ***indocyanin*** ***green*** angiography (ICGA) offers detailed two-dimensional imaging of choroidal pathologies. However, the spatial extension of lesions is not reproduced. We developed a novel method for three-dimensional documentation of choroidal vascular abnormalities. METHODS: Focal series were performed using a laser scanning ophthalmoscope (Heidelberg Retina Angiograph). Thirty-two images within a distance of 4 mm were taken at a frequency of 20 Hz. Following correction of dislocation, a surface of normalized ***fluorescence*** ***intensity*** was determined and displayed topographically. RESULTS: In physiological eyes three-dimensional ICGA demonstrates the homogeneous concavity of the choroid with prominent overlay of retinal vessels. Classic choroidal neovascularization (CNV) imposes as substantial elevation. Occult CNV are demarcated despite negative conventional ICGA due to reduction of blocking phenomena. Therapeutic interventions such as photocoagulation, photodynamic therapy and surgery induce a resolution of CNV with or without residual defects within the choroidal pattern. CONCLUSION: Topographic ICGA allows for the first time in-vivo representation of prominence and depth of vascularized pathologies and provides a tool for improved diagnostic and therapeutic evaluation.

L24 ANSWER 14 OF 42 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 1999349332 MEDLINE
DOCUMENT NUMBER: 99349332 PubMed ID: 10420847
TITLE: Imaging of spontaneous canine mammary tumors using fluorescent contrast agents.
AUTHOR: Reynolds J S; Troy T L; Mayer R H; Thompson A B; Waters D J; Cornell K K; Snyder P W; Sevick-Muraca E M
CORPORATE SOURCE: School of Chemical Engineering, Purdue University, West Lafayette, IN 47907, USA.
CONTRACT NUMBER: K04CA68374 (NCI)
R01CA67176 (NCI)
SOURCE: PHOTOCHEMISTRY AND PHOTOBIOLOGY, (1999 Jul) 70 (1) 87-94. Journal code: 0376425. ISSN: 0031-8655.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990827
Last Updated on STN: 19990827
Entered Medline: 19990818

AB We present near-infrared frequency-domain photon migration imaging for the lifetime sensitive detection and localization of exogenous fluorescent contrast agents within tissue-simulating phantoms and actual tissues. We employ intensity-modulated excitation light that is expanded and delivered to the surface of a tissue or tissue-simulating phantom. The ***intensity*** -modulated ***fluorescence*** generated from within the volume propagates to the surface and is collected using a gain-modulated image-intensified charge-coupled device camera. From the spatial values of modulation amplitude and phase of the detected fluorescent light, micromolar volumes of diethylthiatricarbocyanine iodide (tau = 1.17 ns) and ***indocyanine*** ***green*** (***ICG***) (tau = 0.58 ns) embedded 1.0 cm deep in a tissue phantom are localized and discriminated on the basis of their lifetime differences. To demonstrate the utility of frequency-domain fluorescent measurements for imaging disease, we image the fluorescence emitted from the surface of in vivo and ex vivo canine mammary gland tissues containing lesions with preferential uptake of ***ICG*** . Pathology confirms the ability to detect spontaneous mammary tumors and regional lymph nodes amidst normal mammary tissue and fat as deep as 1.5 cm from the tissue surface.

L24 ANSWER 15 OF 42 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:197682 CAPLUS
DOCUMENT NUMBER: 128:267965
TITLE: Immunohistochemical staining composition
INVENTOR(S): Shibamura, Seiichi; Ito, Susumu; Takesako, Kazuhiro; Irimura, Tatsuro

PATENT ASSIGNEE(S): Daiichi Pure Chemicals Co., Ltd., Japan; Shibamura, Seiichi; Ito, Susumu; Takesako, Kazuhiro; Irimura, Tatsuro
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9812560	A1	19980326	WO 1997-JP3306	19970918
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9743188	A1	19980414	AU 1997-43188	19970918
AU 719676	B2	20000518		
EP 935139	A1	19990811	EP 1997-941192	19970918
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
CN 1238042	A	19991208	CN 1997-199808	19970918
NO 9901317	A	19990519	NO 1999-1317	19990318
US 2002028474	A1	20020307	US 2001-920805	20010803

PRIORITY APPLN. INFO.: JP 1996-246782 A 19960919
JP 1996-347886 A 19961226
JP 1997-45516 A 19970228
WO 1997-JP3306 W 19970918
US 1999-147839 B1 19990617

AB An immunohistochem. staining compn. contains a diagnostic marker contg. an antibody having a fluorescent functional group and a substance selected from the group consisting of glycerophospholipids, fatty acids and sugar derivs. serving as a surfactant. Glycerophospholipids are acylglycerol phosphate, in particular 1,2-diacyl-sn-glycerol 3-phosphate such as dimyristoyl or distearoylphosphatidic acid or acylglycerol phosphocholine, in particular 1,2-diacyl-sn-glycerol 3-phosphocholine such as distearoylphosphatidylcholine. The sugar deriv. is octyl glucoside and the fluorescent functional group is one derived from ***indocyanine*** ***green*** -N-hydroxysuccinimide ester. Glycerophospholipids, fatty acids, or sugar derivs. serves as an enhancer of ***fluorescence*** ***intensity*** for diagnostic marker of immunohistochem. staining contg. the antibody bonded to fluorescent functional group. The antibody is anti-cancer antibody. The compn. is excellent in ***fluorescence*** ***intensity*** and is free from the fear of damages to biol. tissues or DNAs caused by UV excitation, thus being useful for biol. immunohistochem. staining. The compn. makes it possible to efficiently and safely conduct, for example, the quasi-intracorporeal early diagnosis of malignant neoplasm of the epithelial tissues, such as esophageal carcinoma, gastric cancer or colon cancer, with an IR endoscope and the specification and diagnosis of foci in a surgical operation.

L24 ANSWER 16 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 12
ACCESSION NUMBER: 1998:509726 BIOSIS
DOCUMENT NUMBER: PREV199800509726
TITLE: Kinetic determination of total casein in milk and dairy products by long-wavelength fluorescence detection.
AUTHOR(S): Aguilar-Caballos, Maria Paz; Gomez-Hens, Agustina; Perez-Bendito, Dolores (1)
CORPORATE SOURCE: (1) Dep. Analytical Chem., Fac. Sci., Univ. Cordoba, E-14004 Cordoba Spain
SOURCE: Journal of Agricultural and Food Chemistry, (Oct., 1998) Vol. 46, No. 10, pp. 4250-4254.
ISSN: 0021-8561.

DOCUMENT TYPE: Article
LANGUAGE: English
AB A very simple and fast fluorometric method for the routine determination of total casein in food samples is described. It is based on the application of kinetic methodology to the ***Indocyanine*** ***Green*** -cetyltrimethylammonium bromide-casein system by using stopped-flow mixing technique and long-wavelength fluorescence measurements, which allow the temporal and spectral discrimination of the analytical signal. The electrostatic interaction between casein and the surfactant eliminates the quenching caused by the latter on the fluorescence of the dye, so that the ***fluorescence*** ***intensity*** increment with time, which is measured in apprx 2 s, is directly related to casein concentration. The dynamic range of the calibration graph is 3-100 mug mL-1, and the detection limit is 0.9 mug mL-1. The relative standard deviation is <2%. The proposed method was applied to the determination of total casein in milk samples and dairy products with a recovery of 96.8-103.1%.

L24 ANSWER 17 OF 42 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:625594 CAPLUS
DOCUMENT NUMBER: 129:303687
TITLE: Near-IR electrogenerated chemiluminescence of tricarbocyanine dyes in micellar systems
AUTHOR(S): Lee, Sang Kwon; Bard, Allen J.
CORPORATE SOURCE: Dep. Chem. and Biochemistry, The Univ. Texas at Austin, Austin, TX, 78712, USA
SOURCE: Analytical Letters (1998), 31(13), 2209-2229
CODEN: ANALBP; ISSN: 0003-2719
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two tricarbocyanine near-IR dyes contg. the same (1,1-dimethylbenz[e]indole) heterocyclic nuclei, IR144 and IR125, were studied in org. solvents, in water, and in the presence of certain surfactants. The anodic oxidn. of IR144 produces electrogenerated chemiluminescence (ECL) in the presence of tri-n-propylamine as a coreactant in sodium dodecyl sulfate surfactant soln. or in MeCN/DMSO (2:1 vol./vol.) soln. The one-electron oxidn. of IR144 generated the corresponding fairly stable radical cation at +0.48 V vs Ag/AgCl in MeCN/DMSO (2:1). In the micelle system, the potential was shifted to a more pos. potential, +1.1 V vs Ag/AgCl, as found by differential pulse voltammetry. The ECL intensity for IR125 was much weaker than that of IR144, and the potential did not change in water or surfactant soln. The absorption spectra indicated extensive dimerization for IR144 in aq. soln., while IR125 showed little evidence of dimerization. For IR144, the ***fluorescence*** ***intensity*** in water decreased dramatically when compared to both org. solvents MeOH and MeCN. In all the aq. surfactant solns., the ***fluorescence*** ***intensity*** is partially restored. These micelle ECL reactions should be useful in the design of new labels for ECL applications.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 18 OF 42 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 1999051679 MEDLINE
DOCUMENT NUMBER: 99051679 PubMed ID: 9834614
TITLE: A case of choroidal metastasis from bronchial atypical carcinoid tumor (well-differentiated neuroendocrine cell carcinoma).
AUTHOR: Abe S; Nishikatsu H; Yasui T; Mochizuki M
CORPORATE SOURCE: Department of Ophthalmology, Iwaki Kyoritsu General Hospital, Japan.
SOURCE: NIPPON GANKA GAKKAI ZASSHI. ACTA SOCIETATIS OPHTHALMOLOGICAE JAPONICAE, (1998 Oct) 102 (10) 698-703.
Journal code: 7505716. ISSN: 0029-0203.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980507
Last Updated on STN: 19980507
Entered Medline: 19980428

AB This study reinvestigates the spectral properties of ***ICG*** (***Indocyanine*** ***green***) in vivo, the role of quenching, and the possibility of an interaction of ***ICG*** with blood components and/or vessel walls. ***ICG*** quenching as a function of concentration was studied by spectrophotometry on whole blood samples from golden hamsters. Fluorescence ***ICG*** characteristics were evaluated by front-face fluorometry. In vivo, fluorescence measurements were performed on the femoral artery of golden hamsters. In vitro, on whole blood samples, ***fluorescence*** ***intensity*** is modified by ***ICG*** quenching as concentration increases above 80 microgram/ml. The maximum fluorescence peak is not affected and remains centered at 832 nm. The in vivo measurements display a similar ***fluorescence*** ***intensity*** shape, which is affected only by ***ICG*** concentrations. However, the maximum fluorescence emission peak is modified significantly with time. Between 0 and 120 min, four phases can be distinguished in which a wavelength shift from 826 to 835 nm is observed. The wavelength shift with change in ***fluorescence*** ***intensity*** observed in vivo could be due to a localization of ***ICG*** molecules in sites more hydrophobic than serum proteins. It is possible to hypothesize the presence of an endothelium-bound form with a specific fluorescence spectrum. The amphiphilic properties of ***ICG*** are consistent with fixation of some ***ICG*** molecules on sites other than plasmatic proteins after injection. The process of fixation of ***ICG*** molecules on surface components or within the vascular endothelium could be due to a change in the microenvironment of some ***ICG*** molecules.

L24 ANSWER 21 OF 42 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 1998050860 MEDLINE
DOCUMENT NUMBER: 98050860 PubMed ID: 9390494
TITLE: Biodistribution of ***indocyanine*** ***green*** in a porcine burn model: light and fluorescence microscopy.
AUTHOR: Schomacker K T; Torri A; Sandison D R; Sheridan R L; Nishioka N S
CORPORATE SOURCE: Massachusetts General Hospital, Department of Dermatology, Harvard Medical School, Boston 02114, USA.
SOURCE: JOURNAL OF TRAUMA, (1997 Nov) 43 (5) 813-9.
Journal code: 0376373. ISSN: 0022-5282.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971218

AB BACKGROUND: Infrared-excited fluorescence of intravenously administered ***indocyanine*** ***green*** (***ICG***) is being used as a method of early determination of burn depth. METHODS: Fluorescence microscopy and tissue fluorescence were recorded in a porcine burn model and correlated to burn severity and age. RESULTS: Recently placed superficial burns show significant fluorescence compared with adjacent normal tissue as a result of a strong inflammatory reaction in the superficial dermis with minimal vascular occlusion. The magnitude of the inflammatory reaction decreases with time. For deeper burns, vascular occlusion prevents transport of ***ICG*** into the burn and the ***intensity*** of ***ICG*** ***fluorescence*** in burn eschar is negligible. CONCLUSION: The ***intensity*** of ***ICG***

fluorescence measured at the surface of the wound for burns of similar age was shown to decrease exponentially with the depth of the burn. The enhanced fluorescence of partial-thickness burns is attributable to increased permeability, and the decreased signal associated with deeper injuries is attributable to vascular occlusion. These results suggest that it is possible to differentiate burns that will heal spontaneously with minimal granulation from those that will not by measuring the ***intensity*** of ***ICG*** ***fluorescence*** .

L24 ANSWER 22 OF 42 MEDLINE DUPLICATE 17
ACCESSION NUMBER: 1998006206 MEDLINE
DOCUMENT NUMBER: 98006206 PubMed ID: 9347983
TITLE: Noninvasive optical imaging of the subarachnoid space and cerebrospinal fluid pathways based on near-infrared fluorescence.
AUTHOR: Sakatani K; Kashiwasake-Jibu M; Taka Y; Wang S; Zuo H; Yamamoto K; Shimizu K
CORPORATE SOURCE: Department of Neurosurgery, China-Japan Friendship Hospital, Beijing, China.
SOURCE: JOURNAL OF NEUROSURGERY, (1997 Nov) 87 (5) 738-45. Journal code: 0253357. ISSN: 0022-3085.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971105
AB The authors have developed a noninvasive optical method to image the subarachnoid space and cerebrospinal fluid pathways in vivo based on the near-infrared fluorescence of ***indocyanine*** ***green*** (***ICG***). The ***ICG*** was bound to purified lipoproteins (***ICG*** -lipoprotein) and injected into the subarachnoid space of neonatal and adult rats. The ***ICG*** fluorescence was detected by a cooled charge-coupled device camera. After injection of ***ICG*** -lipoprotein into the cerebral subarachnoid space of the neonatal rat, ***ICG*** fluorescence was clearly detected at the injection site through the skull and skin. The ***ICG*** fluorescence was observed in the cerebellum and the lumbar spinal cord 1 and 8 hours postinjection, respectively. After injection of ***ICG*** -lipoprotein into the lumbar spinal subarachnoid space of an adult rat, ***ICG*** fluorescence was observed from the injection site to the thoracic levels along the spinal subarachnoid space. In addition, with the rat's head tilted downward, ***ICG*** fluorescence had extended to the cerebral subarachnoid space by 1 hour postinjection. The ***ICG*** fluorescence imaging of the cerebral subarachnoid space demonstrated an increase in ***fluorescence*** ***intensity*** around the lambdoid suture and the forebrain. On dissection of the rat brain the former location was identified as the supracerebellar cistern and the latter as the olfactory cistern. The results of this study are the first to demonstrate that an optical technique is applicable to imaging of the subarachnoid space and cerebrospinal fluid pathways in vivo. In addition, ***ICG*** -lipoprotein provides a sensitive optical tracer for imaging extravascular biological structures. Finally, ***ICG*** fluorescence imaging does not require an intricate imaging system because ***ICG*** is localized near the surface of the body.

L24 ANSWER 23 OF 42 MEDLINE DUPLICATE 18
ACCESSION NUMBER: 97098338 MEDLINE
DOCUMENT NUMBER: 97098338 PubMed ID: 8942879
TITLE: Pre-injection fluorescence in ***indocyanine*** ***green*** angiography.
AUTHOR: Piccolino F C; Borgia L; Zinicola E; Iester M; Torrielli S
CORPORATE SOURCE: University Eye Clinic of Genoa, Italy.
SOURCE: OPHTHALMOLOGY, (1996 Nov) 103 (11) 1837-45. Journal code: 7802443. ISSN: 0161-6420.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961220

AB PURPOSE: To verify whether infrared pre-injection fluorescence can be observed in patients undergoing ***indocyanine*** ***green*** (***ICG***) angiography. METHODS: Infrared fundus photographs were taken before dye injection for 450 consecutive patients undergoing ***ICG*** angiography for different chorioretinal disorders. The authors used a high-resolution videoangiography system with the standard ***ICG*** filters inserted (overlap, < 0.5%) and the highest flash ***intensity*** . RESULTS: Pre-injection ***fluorescence*** was detected in 184 patients (40.8%). It was a strong fluorescence in 75 patients (40.7%) and a faint fluorescence in 109 (59.2%). When fluorescence was strong, it simulated vascular filling on the ***ICG*** angiogram. Pre-injection fluorescence resulted from the following lesions: (1) old grayish subretinal hemorrhages (35 patients); (2) lipofuscin-like deposits (65 patients); (3) pigmented choroidal neovascular membranes (72 patients); and (4) serous retinal detachments lasting from several months or years (12 patients). Highly reflecting white lesions were not fluorescent. CONCLUSION: Pre-injection fluorescence of chorioretinal lesions is frequently detectable in patients with diseases requiring ***ICG*** examination. A pre-injection photograph may help to avoid misinterpretation of the angiograms. The authors' findings may be interpreted as pseudofluorescence or autofluorescence. Pigments contained in pathologic structures of the ocular fundus may be the source of autofluorescence emissions in the near-infrared range.

L24 ANSWER 24 OF 42 MEDLINE DUPLICATE 19
ACCESSION NUMBER: 97186313 MEDLINE
DOCUMENT NUMBER: 97186313 PubMed ID: 9033888
TITLE: [Control of photocoagulation intensity by thermo-induced release of a fluorescent marker encapsulated in liposomes: study of an in vivo vascular model].
Controle de l'intensite des photocoagulations par liberation thermo-induite d'un marqueur fluorescent encapsule dans des liposomes: etude d'un modele vasculaire in vivo.
AUTHOR: Desmettre T; Mordon S; Soulie S; Devoisselle J M; Mitchell V
CORPORATE SOURCE: INSERM Unite 279, CH&U, Lille.
SOURCE: JOURNAL FRANCAIS D OPHTALMOLOGIE, (1996) 19 (11) 667-78.
Journal code: 7804128. ISSN: 0181-5512.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970321
Last Updated on STN: 19970321
Entered Medline: 19970313

AB PURPOSE: To evaluate the feasibility of thermal damage assessment of blood vessels by using laser-induced release of liposome-encapsulated dye. METHODS: A skin flap window model of aluminium was implanted on the loose skin on the back of adults Golden hamsters to expose skin blood vessels in vivo. Thermosensitive liposomes (DSPC) loaded with 5,6-Carboxyfluorescein were injected together with a specific ***Indocyanine*** ***green*** (***ICG***) formulation (O/W emulsion) in order to enhance diode laser absorption. Photocoagulations were then performed on the vessels with a diode laser (lambda = 810 nm, P = 0.8W, phi = 1.3 mm, 1 to 6s). Fluorescence measurements were realized with an ultra high sensitivity intensified camera (Hamamatsu Argus 50 imaging system). RESULTS: Two different ***fluorescence*** ***intensity*** curves corresponding

fluorescence measurement of laser-induced release of liposome-encapsulated dye is clearly demonstrated. This procedure could conceivably prove useful for controlling the thermal coagulation of biological tissues.

L24 ANSWER 26 OF 42 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:204983 CAPLUS
DOCUMENT NUMBER: 124:311510
TITLE: Intravital near-infrared fluorescence microscopy with ***indocyanine*** ***green*** to visualize deep tissue microcirculation
AUTHOR(S): Ohshima, Norio; Homma, Satoshi; Yanagi, Kennichi; Sato, Masaaki; Ito, Takayuki; Wayland, Harold
CORPORATE SOURCE: Institute Basic Medical Sciences, University Tsukubo, Tsukuba, 305, Japan
SOURCE: Tissue Perfusion and Organ Function (1996), 15-27. Editor(s): Kamada, Takenobu; Shiga, Takeshi; McCuskey, Robert S. Elsevier: Amsterdam, Neth. CODEN: 62NYAN
DOCUMENT TYPE: Conference
LANGUAGE: English
AB ***Indocyanine*** ***green*** (***ICG***) is a dye that emits fluorescence in the near-IR region. Since light of longer wavelengths is less scattered by tissue than shorter ones, ***ICG*** fluorescence microscopy is expected to be a promising method to provide more detailed information on deep tissue blood circulation than other fluorochromes, say, fluorescein. We constructed a near-IR microscope system to enable intravital observation and proper detection of ***ICG*** fluorescence. By in vitro calibration expts., it was confirmed that the ***intensity*** of ***fluorescence*** showed a max. value over an ***ICG*** concn. range from 100 .mu.g/mL to 300 .mu.g/mL. Microvessels of the skeletal muscles and disseminated tumor in the mesentery of rats were subjected to intravital microscopic observation using this system. Microvascular images with a good contrast against background were obtained.

L24 ANSWER 27 OF 42 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 21
ACCESSION NUMBER: 95269983 EMBASE
DOCUMENT NUMBER: 1995269983
TITLE: Changes in ***intensity*** of ***fluorescence*** in drusen during ***indocyanine*** ***green*** angiography.
AUTHOR: Kamo M.; Shiraki K.; Moriwaki M.; Miki T.
CORPORATE SOURCE: Department of Ophthalmology, Kita Municipal Hospital, 5-4-8 Nishikujo,Konohana-ku, Osaka 554, Japan
SOURCE: Japanese Journal of Clinical Ophthalmology, (1995) 49/5 (885-889). ISSN: 0370-5579 CODEN: RIGAA3
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
012 Ophthalmology
LANGUAGE: Japanese
SUMMARY LANGUAGE: English; Japanese
AB We performed ***indocyanine*** ***green*** angiography in 17 eyes with drusen and age- related macular degeneration. The findings were analyzed by image processing, or region mapping, using an IMAGEnet system. Fluorescence of drusen showed various changes in intensity as compared with the surrounding area during the course of angiography. The observed changes appeared to be due to differences in components of individual drusen.

L24 ANSWER 28 OF 42 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:709289 CAPLUS
DOCUMENT NUMBER: 123:164107
TITLE: Fluorescence measurement of diode (805nm) laser-induced release of 5,6-CF from DSPC liposomes for monitoring of temperature: An in-vivo study in rat

liver using ***indocyanine*** ***green*** potentiation
AUTHOR(S): Mordon, Serge; Desmettre, Thomas; Devoisselle, Jean Marie; Soulie, Sylvie
CORPORATE SOURCE: INSERM U. 279-ITM, Chandu, Lille, 59037, Fr.
SOURCE: Proceedings of SPIE-The International Society for Optical Engineering (1995), 2391(Laser-Tissue Interaction VI), 475-83
CODEN: PSISDG; ISSN: 0277-786X
PUBLISHER: SPIE-The International Society for Optical Engineering
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This in-vivo study examines the validity of fluorescence measurement of laser-induced release of temp. sensitive liposome-encapsulated dye for monitoring of temp. and prediction of tissue thermal damage. It is performed in rat liver after i.v. injection of liposomes loaded with a fluorescent dye and i.v. injection of ***Indocyanine*** ***Green*** (***ICG***) for diode laser potentiation. Temp. sensitive liposomes (DSPC: Di-Stearoyl-Phosphatidyl-Choline) are loaded with 5,6-Carboxyfluorescein (5,6-CF). These liposomes (1.5mL soln.) and ***ICG*** (1.5mL soln.-5mg/kg) are injected to adult male wistar rats. Two hours later, the liver is exposed and irradiated with a 0.8 W diode laser using pulses lasting from 1s to 6s (fluence ranging from 16 to 98 J/cm2). Simultaneously, the fluorescence emission is measured with a fluorescent imaging system. Results show that the ***fluorescence*** ***intensity*** increases linearly from 18J/cm2 up to 75J/cm2. These fluences correspond to surface temps. between 42.degree.C to 64.degree.C. The measurements appear to be highly reproducible. In this temp. range, the accuracy is +/- 3.degree.C. The max. intensity is obsd. immediately after the laser is switched off and a decrease of the ***fluorescence*** ***intensity*** is obsd. (27% in 20 min) due to the 5,6-CF clearance. However, the ratio (IF/Ibck) remains almost stable over this period of time and the detn. of the temp. is still possible with a good accuracy even 20 min after laser irradn. In conclusion, temp. monitoring by using fluorescence measurement of laser-induced release of liposome-encapsulated dye is clearly demonstrated. This procedure could conceivably prove useful for controlling the thermal coagulation of biol. tissues.

L24 ANSWER 29 OF 42 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 22
ACCESSION NUMBER: 94060488 EMBASE
DOCUMENT NUMBER: 1994060488
TITLE: Characteristics of choroidal fluorescence in infrared fundus angiography.
AUTHOR: Iida T.; Muraoka K.; Hagimura N.; Kishi S.; Tanaka T.
CORPORATE SOURCE: Department of Ophthalmology, Gunma University School of Medicine, 2 Showa machi,Maebashi 371, Japan
SOURCE: Japanese Journal of Clinical Ophthalmology, (1994) 48/1 (85-92).
ISSN: 0370-5579 CODEN: RIGAA3
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We made in vitro and in vivo experiments on fluorescence from ***indocyanine*** ***green*** (***ICG***) and fluorescein sodium. Either solution was placed in two overlying flat glass chambers. The ***intensity*** of ***fluorescence*** from ***ICG*** (0.03 mg/ml) increased linearly up to the depth of 400 .mu.m. The fluorescence from fluorescein (0.75 mg/ml) remained constant independent of the depth of the solution. In clinical fundus angiography, ***ICG*** showed more intense fluorescence at the site of arteriovenous crossings, major choroidal vessels and choroidal angiomas. The choriocapillaris appeared as uniform background fluorescence. This feature allowed estimation of the patency of the choriocapillaris as distinct from deeper choroidal layers. Fluorescence by ***ICG*** angiography was thus dependent on the added

sum of ***ICG*** contained in the area of observation, while that by fluorescein angiography tended to show the most superficial dye-containing layar because of saturation effect.

L24 ANSWER 30 OF 42 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94340702 EMBASE
DOCUMENT NUMBER: 1994340702
TITLE: Dynamic fluorescence angiography with ***indocyanine*** ***green*** for the assessment of intestinal perfusion.
AUTHOR: Kasperk R.; Rubben A.; Schumpelick V.
CORPORATE SOURCE: Department of Surgery, University Clinic RWTH, Pauwelsstrasse 30,D-52057 Aachen, Germany
SOURCE: Research in Surgery, (1994) 6/1 (6-9).
ISSN: 0214-5987 CODEN: RSURES
COUNTRY: Spain
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 009 Surgery
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Tissue perfusion in the rat stomach was studied to determine the experimental feasibility and possible disadvantages of the technique. Twenty rats underwent laparotomy and exposure of the stomach. In 10 of them the esophagogastric junction was transsected and the proximal stomach devascularized. Tissue fluorescence after three consecutive intravenous applications of 1 mg/kg ***indocyanine*** ***green*** was captured by a videocamera, analyzed densitometrically and plotted as ***fluorescence*** ***intensity*** -time diagrams. ***Fluorescence*** kinetics with the key parameters of maximum intensity, time point of maximum intensity and increase per time delineate typical differences in areas of high and low tissue perfusion with excellent spatial resolution. ***Indocyanine*** ***green*** adheres temporarily to internal vessel walls, causing accumulation of fluorescence with rapidly repeated dye administrations. Due to its practicability and its dynamic and non-invasive character, fluorescence videoangiography with ***indocyanine*** ***green*** possesses potential utility in the experimental field.

L24 ANSWER 31 OF 42 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93206071 EMBASE
DOCUMENT NUMBER: 1993206071
TITLE: A novel fluorescence ratiometric method confirms the low solvent viscosity of the cytoplasm.
AUTHOR: Luby-Phelps K.; Mujumdar S.; Mujumdar R.B.; Ernst L.A.; Galbraith W.; Waggoner A.S.
CORPORATE SOURCE: Dept. of Physiology, University of Texas SW Medical Ctr., 5323 Harry Hines Blvd.,Dallas, TX 75235-9040, United States
SOURCE: Biophysical Journal, (1993) 65/1 (236-242).
ISSN: 0006-3495 CODEN: BIOJAU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
027 Biophysics, Bioengineering and Medical Instrumentation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Two homologous indocyanine dyes, Cy3.18 and Cy5.18, can be used as a ratio pair for fluorometric determination of solvent viscosity. Succinimidyl ester derivatives of these dyes can be attached to inert carrier macromolecules, such as Ficoll 70, for measurement of intracellular or intravesicular solvent viscosity. When the viscosity of the solvent was varied by various methods, the ***fluorescence*** ***intensity*** ratio (Cy3/Cy5) in a mixture of Cy3.18-Ficoll 70 (Cy3F70) and Cy5.18-Ficoll 70 (Cy5F70) in solution was found to be solely a function of solvent viscosity and was insensitive to other solvent parameters such as dielectric constant, temperature, and the ability of the solvent to form

hydrogen bonds. Most important, it was insensitive to the presence of large macromolecules, such as proteins, which increase the shear viscosity but have little effect on solvent viscosity. Following microinjection into the cytoplasm of living tissue culture cells, no binding of Cy3F70 or Cy5F70 to intracellular components was detected by fluorescence recovery after photobleaching. ***Fluorescence*** ***intensity*** ratio imaging of Cy3F70 and Cy5F70 in nonmotile interphase CV1 and PtK1 cells showed that the solvent viscosity of cytoplasm was not significantly different from water and showed no spatial variation.

L24 ANSWER 32 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1993:484109 BIOSIS
DOCUMENT NUMBER: PREV199396117709
TITLE: Photoactivable fluorophores for the measurement of fluence in turbid media.
AUTHOR(S): Lilge, L. (1); Flotte, T. J.; Kochevar, I. E.; Jacques, S. L.; Hillenkamp, F.
CORPORATE SOURCE: (1) Room 419, Hamilton Regional Cancer Center, 699 Concession St., Hamilton, ON L8V 5C2 Canada
SOURCE: Photochemistry and Photobiology, (1993) Vol. 58, No. 1, pp. 37-44.
ISSN: 0031-8655.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Knowledge of the fluence distribution in biological tissue is essential for applications of lasers and light in medicine. A method using a photoactivable fluorophore as a chemical actinometer is presented to investigate the fluence (J/cm-2) distribution in tissue-simulating phantoms. Such a chemical actinometer provides high spatial resolution (ltoreq 20 mu-m) while minimizing the disturbance of the fluence distribution. The actinometer substance, nonfluorescent in its native state, is incorporated into an acrylamide gel. Upon absorption of 351 nm radiation (lambda-act), the actinometer substance becomes a fluorophore, which is excited at lambda-ex ltoreq 485 nm. Thus, the spatial distribution of the emitted fluorescence (lambda-em gtoreq 515 nm) in the actinometer represents the fluence distribution of the activating radiation. Using histological techniques, 20 mu-m sections are cut from gel-like optical phantoms containing the actinometric substance. The ***fluorescence*** ***intensity*** in the section is recorded under a standard fluorescence microscope equipped with a sensitive video camera. To simulate different biological tissues, the scattering and absorption properties of the gel phantoms are varied over a wide range. The experimentally obtained fluence distributions are compared with theoretical models of light distribution in turbid media.

L24 ANSWER 33 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:332467 BIOSIS
DOCUMENT NUMBER: BA94:34308
TITLE: ***INDOCYANINE*** ***GREEN*** FUNDUS ANGIOGRAPHY IN HIGH MYOPIA.
AUTHOR(S): SHIRAKI K; MORIWAKI M; KAMO M; MATSUMOTO M; SAKAMOTO T; YAMORI Y; MIKI T
CORPORATE SOURCE: DEP. OPHTHALMOL., OSAKA CITY UNIV. MEDICAL SCH. 1-5-7, ASAHI-MACHI, ABENO-KU, OSAKA, 545, JAPAN.
SOURCE: JPN J CLIN OPHTHALMOL, (1992) 46 (3), 229-231.
CODEN: RIGAA3. ISSN: 0370-5579.
FILE SEGMENT: BA; OLD
LANGUAGE: Japanese
AB We performed ***indocyanine*** ***green*** (***ICG***) fundus angiography in 15 eyes of 8 cases with high myopia of -6 diopters or more. We used fundus camera 50 IA by Topcon. We observed disappearance of choroidal vessels in area of choroidal patchy atrophy and of chorioretinal degenerations. In areas of patchy atrophy, there were occassionally remnants of choroidal vessels located deeper in the choroid than shown by conventional fluorescein angiography. There was an eye of high ***intensity*** of ***fluorescence*** persistent throughout the late venous phase without manifest dye leakage. This finding was suggestive of

occult choroidal neovascularization. ***ICG*** angiography thus supplied more accurate informations concerning the disturbed state of circulation in high myopia.

L24 ANSWER 34 OF 42 MEDLINE DUPLICATE 23
ACCESSION NUMBER: 92152897 MEDLINE
DOCUMENT NUMBER: 92152897 PubMed ID: 1739286
TITLE: Burn depth estimation using ***indocyanine*** ***green*** fluorescence.
AUTHOR: Green H A; Bua D; Anderson R R; Nishioka N S
CORPORATE SOURCE: Harvard Medical School, Department of Dermatology, Massachusetts General Hospital, Boston 02114.
SOURCE: ARCHIVES OF DERMATOLOGY, (1992 Jan) 128 (1) 43-9. Journal code: 0372433. ISSN: 0003-987X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199203
ENTRY DATE: Entered STN: 19920405
Last Updated on STN: 19920405
Entered Medline: 19920319
AB Expedient primary excision of deep dermal and full-thickness burn wounds with subsequent skin grafting is the standard of care in most burn institutions, but differentiating full-thickness from partial-thickness burns is often difficult. Because accurate early assessment of burn depth may improve care, a variety of technical methods have attempted to measure burn depth but these methods have had limited success. We describe a new technique to determine burn depth that uses infrared (840- to 850-nm) fluorescence emission from intravenously administered ***indocyanine*** ***green*** following excitation with infrared (780 nm) and UV light (369 nm). Full-thickness and partial-thickness burns in hairless rat skin were distinguished based on the infrared-induced and UV-induced ***fluorescence*** ***intensity*** ratios relative to normal, unburned skin immediately after the burn and on post-burn days 1 through 3 and 7. Dual-wavelength excitation of ***indocyanine*** ***green*** infrared fluorescence can delineate full-thickness from partial-thickness burns at an early date, allowing prognosis, surgical planning, and early primary excision and grafting.

L24 ANSWER 35 OF 42 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 24
ACCESSION NUMBER: 88149183 EMBASE
DOCUMENT NUMBER: 1988149183
TITLE: Semiconductor laser fluorimetry for enzyme and enzymatic assays.
AUTHOR: Imasaka T.; Okazaki T.; Ishibashi N.
CORPORATE SOURCE: Faculty of Engineering, Kyushu University, Fukuoka 812, Japan
SOURCE: Analytica Chimica Acta, (1988) 208/1-2 (325-329). ISSN: 0003-2670 CODEN: ACACAM
COUNTRY: Netherlands
DOCUMENT TYPE: Journal
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Near-infrared semiconductor laser fluorimetry is applied to assays of xanthine and xanthine oxidase. The fluorescences of ***indocyanine*** ***green*** in the near-infrared region is quenched by hydrogen peroxide. Xanthine is converted to uric acid by xanthine oxidase, in a reaction which also produces hydrogen peroxide; xanthine can be determined by measuring the decrease in ***fluorescence*** ***intensity*** of the dye added to the sample solution. The calibration graph for xanthine is linear from 5x10-5 M to 5 x 10-7 M. The enzyme activity can also be determined.

L24 ANSWER 36 OF 42 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1978:166241 CAPLUS

DOCUMENT NUMBER: 88:166241
TITLE: Fluorescence properties of ***indocyanine*** ***green*** as related to angiography
AUTHOR(S): Benson, R. C.; Kues, H. A.
CORPORATE SOURCE: Appl. Phys. Lab., Johns Hopkins Univ., Laurel, MD, USA
SOURCE: Physics in Medicine & Biology (1978), 23(1), 159-63
CODEN: PHMBA7; ISSN: 0031-9155
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The fluorescence spectrum of ***indocyanine*** ***green*** (***ICG***) was measured as a function of dye concn. in human whole blood as well as in common solvents (H2O, 2H2O, MeOH, MeO2H, DMSO) to det. fluorescence properties unique to ***ICG*** in blood. The undild. whole blood contained anticoagulant citrate phosphate dextrose soln. In the fluorescence app. used, fluorescence was detected in a direction parallel to the excitation light (765 nm) instead of at a 90.degree. angle; this minimized self-absorption of fluorescence at high ***ICG*** concns. Details are given of the app., which was designed to study dyes for use in ophthalmol. The quantum yields of ***ICG*** in the various solvents were measured relative to Na fluorescein in distd. water. The fluorescence max. of ***ICG*** in blood and aq. solns. were 830 and 820 nm, resp. There was a concn. dependence of ***ICG*** fluorescence in blood, and a definite shoulder was obsd. in the concn.-***fluorescence*** ***intensity*** curve that did not appear in other solvents and may be related to ***ICG*** binding by plasma proteins. Fluorescence wavelength, quantum yield, and ***ICG*** concns. needed to achieve max. fluorescence intensities all depended on the solvent used. Fluorescence quenching was apparently due to the aggregation of dye mols.

L24 ANSWER 37 OF 42 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 78364034 EMBASE
DOCUMENT NUMBER: 1978364034
TITLE: Angiography with new dyes.
AUTHOR: Hochheimer B.F.; D'Anna S.A.
CORPORATE SOURCE: Appl. Phys. Lab., Johns Hopkins Univ., Laurel, Md. 20810, United States
SOURCE: Experimental Eye Research, (1978) 27/1 (1-16).
CODEN: EXERA6
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 012 Ophthalmology
014 Radiology
LANGUAGE: English
AB Twelve dyes are shown that may have properties for retinal and choroidal angiography. These dyes are relatively non-toxic and water soluble. Data is given on ***fluorescence*** ***intensity*** and dye decay rates in animal models and angiograms taken with some of these dyes are shown. Additional data is given on five dyes that have been only partially tested.

L24 ANSWER 38 OF 42 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 25
ACCESSION NUMBER: 78167628 EMBASE
DOCUMENT NUMBER: 1978167628
TITLE: Quantification of indicator dye concentration in ocular blood vessels.
AUTHOR: Flower R.W.; Hochheimer B.F.
CORPORATE SOURCE: Johns Hopkins Appl. Phys. Lab., Johns Hopkins Univ. Hosp., Baltimore, Md. 20810, United States
SOURCE: Experimental Eye Research, (1977) 25/2 (103-111).
CODEN: EXERA6
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 012 Ophthalmology
LANGUAGE: English
AB The behavior of an ***indocyanine*** ***green*** (***ICG***) dye bolus as it passes through the ocular blood vessels provides a

calibration standard which permits quantitative dye concentration measurements. Unlike fluorescein, ***ICG*** dye can be delivered to the eye in sufficiently high concentrations by intravenous injection that concentration fluorescence quenching takes place in the ocular blood vessels. The relative maximum ***fluorescence*** ***intensity*** occurring to every blood vessel in which quenching is observed always corresponds to a 0.03 mg/ml dye concentration. Knowing this point and dye concentration in blood as a function of intensity permits routine quantification of dye concentration in blood vessels of the living eye.

L24 ANSWER 39 OF 42 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 26
ACCESSION NUMBER: 78035453 EMBASE
DOCUMENT NUMBER: 1978035453
TITLE: Flow and diffusion of ***indocyanine*** ***green*** and fluorescein dyes in the fovea centralis.
AUTHOR: Riva C.E.; Ben Sira I.; Feke G.T.
CORPORATE SOURCE: Dept. Retina Res., Eye Res. Inst. Retina Found., Boston, Mass. 02114, United States
SOURCE: Experimental Eye Research, (1977) 24/1 (15-23).
CODEN: EXERA6
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
012 Ophthalmology
030 Pharmacology
LANGUAGE: English
AB Fluorescein, a diffusible dye, and ***indocyanine*** ***green*** , a nondiffusible reference substance, were injected into the circulatory system of healthy human subjects with normal ocular functions. A fundus reflectometer simultaneously measured the time course of ***fluorescence*** ***intensity*** of the ***fluorescein*** and the infrared absorption of ***indocyanine*** ***green*** in the fovea centralis. The fluorescein curve represents both the intravascular passage of the dye and its diffusion into the foveal tissue. The ***indocyanine*** ***green*** curve represents only the intravascular passage of ***indocyanine*** ***green*** dye. The difference between the 2 curves provides information on the accumulation of fluorescein in the macula. The characteristics of the fluorescein and ***indocyanine*** ***green*** curves have been determined for subjects with various degrees of ocular pigmentation.

L24 ANSWER 40 OF 42 MEDLINE DUPLICATE 27
ACCESSION NUMBER: 75184117 MEDLINE
DOCUMENT NUMBER: 75184117 PubMed ID: 237570
TITLE: The role of tryptophan residues and hydrophobic interaction in the binding of riboflavin in egg-yolk flavoprotein.
AUTHOR: Steczko J; Ostrowski W
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (1975 May 30) 393 (1) 253-66.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197510
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19970203
Entered Medline: 19751003
AB Egg-yolk flavoprotein has 7.2 tryptophan residues exposed, while the apoprotein shows an apparent exposure of 80 percent of these (5.7 residues) with dimethylsulphoxide as the perturbant. In the apoprotein at pH 6.9 only 4 groups are perturbed to ethylene glycol, 3.2 to glycerol and 1.4 to sucrose. Diminishing estimates of exposure obtained with increasing molecular diameter of the perturbant suggests that part of indole chromophores of apoprotein are located in "crevices" of the protein molecule. The apoprotein was treated with 2-hydroxy-5-nitrobenzyl bromide, H2O2 and N-bromosuccinimide under conditions designed to accomplish modification of tryptophan residues. Five to six of the eight tryptophans

present in the protein were modified. Under these conditions the apoprotein completely looses its capacity for binding riboflavin and the ***fluorescent*** ***intensity*** of the protein at 360 nm is quenched at the same time to about 80 percent of its initial value. The presence of nonpolar amino acid residues on the surface of the apoprotein suggested the importance of hydrophobic interactions as the dominant factor controlling the binding of riboflavin. The hydrophobic probes ***Indocyanine*** ***green*** and 4-benzoylamide-4-aminostilbene-2,2-disulphonic acid bound to the apoprotein giving equimolar complexes with dissocation constants, KD 6.5-10(-7) M and 1.8-10(-6) M, respectively, Addition of an equimolar amount of riboflavin quantitatively displaced these dyes from their complexes with apoprotein as shown by spectrophotometric and spectrofluorometric studies.

L24 ANSWER 41 OF 42 MEDLINE
ACCESSION NUMBER: 75114399 MEDLINE
DOCUMENT NUMBER: 75114399 PubMed ID: 1090558
TITLE: Fluorescein diffusion in the human optic disc.
AUTHOR: Ben-Sira I; Riva C E
SOURCE: INVESTIGATIVE OPHTHALMOLOGY, (1975 Mar) 14 (3) 205-11.
Journal code: 0374730. ISSN: 0020-9988.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197505
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19750527
AB The characteristics of the transcapillary transfer of fluorescein dye in the optic disc of healthy individuals has been studied. A diffusible fluorescein dye and a nondiffusible reference substance, ***indocyanine*** ***green*** (***ICG***), which was assumed to remain in the capillaries, were injected into the circulatory system. The time courses of the concentrations of the two dyes in the optic disc were determined by simultaneously recording the ***fluorescence*** ***intensity*** of ***fluorescein*** and the infrared absorption by ***ICG*** with a fundus reflectometer. The difference between the fluorescein concentration curve and the reference ***ICG*** curve is a measure of the accumulation of fluorescein in the disc tissue. Our measurements indicate that fluorescein dye does not diffuse across the capillaries in the optic disc. The accumulation of fluorescein in the disc only starts at about one minute after the injection and seems to be due to diffusion of the dye from the surrounding choroid. The time constant of this diffusion process was found to be approximately one minute.

L24 ANSWER 42 OF 42 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 76025435 EMBASE
DOCUMENT NUMBER: 1976025435
TITLE: Fluorescein diffusion in the human optic disc.
AUTHOR: Ben Sira I.; Riva C.E.
CORPORATE SOURCE: Dept. Retina Res., Retina Found., Boston, Mass., United States
SOURCE: Investigative Ophthalmology, (1975) 14/3 (205-211).
CODEN: INOPAO
DOCUMENT TYPE: Journal
FILE SEGMENT: 012 Ophthalmology
LANGUAGE: English
AB The characteristics of the transcapillary transfer of fluorescein dye in the optic disc of healthy individuals were studied. A diffusible fluorescein dye and a nondiffusible reference substance, ***indocyanine*** ***green*** (***ICG***), which was assumed to remain in the capillaries, were injected into the circulatory system. The time courses of the concentrations of the 2 dyes in the optic disc were determined by simultaneously recording the ***fluorescence*** ***intensity*** of ***fluorescein*** and the infrared absorption by ***ICG*** with a fundus reflectometer. The difference between the

LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990128
Last Updated on STN: 19990128
Entered Medline: 19990111

AB We describe a case of choroidal metastasis from bronchial atypical carcinoid tumor (well-differentiated neuroendocrine cell carcinoma). In this report, we compared the images of ***indocyanine*** ***green*** infrared fluorescence angiography (IA) to the histological appearance of the metastatic tumor. A 48-year-old male patient presented with metastatic choroidal tumors in both eyes. The IA findings revealed high ***intensity*** of ***fluorescence*** in the center of the tumor, but low intensity at the edge. Afterwards, the patient underwent enucleation of his left eye because of secondary glaucoma. Microscopic examination of the resected eyeball disclosed two histological patterns: one was that of typical carcinoid tumor; the other atypical carcinoid tumor. In addition, the tumor blood vessels had proliferated more densely in the center of the tumor than at the edge. Only two case reports in the English literature, as for as we know, have previously described the precise histological examination of both choroidal metastasis and primary bronchial carcinoid tumor. This case suggests that the extraordinary IA images are caused by the histologic character of the metastatic tumor: 1. rich vascularity, 2. variety of distribution of the tumor vessels.

L24 ANSWER 19 OF 42 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 1998293120 MEDLINE
DOCUMENT NUMBER: 98293120 PubMed ID: 9629475
TITLE: Development of agents for reinforcement of fluorescence on near-infrared ray excitation for immunohistological staining.
AUTHOR: Ito S; Muguruma N; Hayashi S; Taoka S; Bando T; Inayama K; Sogabe M; Okahisa T; Okamura S; Shibata H; Irimura T; Takesako K; Shibamura S
CORPORATE SOURCE: Second Department of Internal Medicine, School of Medicine, University of Tokushima, Japan.. ito@clin.med.tokushima-u.ac.jp
SOURCE: BIOORGANIC AND MEDICINAL CHEMISTRY, (1998 May) 6 (5) 613-8. Journal code: 9413298. ISSN: 0968-0896.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980903
Last Updated on STN: 19980903
Entered Medline: 19980824

AB ***Fluorescence*** ***intensity*** of ***indocyanine*** ***green*** (***ICG***) derivative (***ICG*** -sulfo-OSu) was too low for its use to detect microlesions. Therefore, we examined the effects of reinforcement agents on ***ICG*** -sulfo-OSu labeled antibodies. Solutions of distearoylphosphatic acid sodium salt (DSPA) and octylglucoside (OG) in physiological phosphate buffered saline (PBS) were found to increase the ***intensity*** of ***fluorescence*** of ***ICG*** -sulfo-OSu labeled antibodies, with shift in the fluorescence peak wavelength from 804 to 821 nm.

L24 ANSWER 20 OF 42 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 1998190104 MEDLINE
DOCUMENT NUMBER: 98190104 PubMed ID: 9521889
TITLE: ***Indocyanine*** ***green*** : physicochemical factors affecting its fluorescence in vivo.
AUTHOR: Mordon S; Devoisselle J M; Soulie-Begu S; Desmettre T
CORPORATE SOURCE: Pavillon Vancostenobel, Lille University Hospital, Lille Cedex, 59037, France.
SOURCE: MICROVASCULAR RESEARCH, (1998 Mar) 55 (2) 146-52. Journal code: 0165035. ISSN: 0026-2862.